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STATUS OF THE ARTIFICIAL HEART PROGRAM

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HEARINGS

BEFORE THE

SUBCOMMITTEE ON
INVESTIGATIONS AND OVERSIGHT

OF THE

COMMITTEE ON
SCIENCE AND TECHNOLOGY
HOUSE OF REPRESENTATIVES

NINETY-NINTH CONGRESS

SECOND SESSION

FEBRUARY 5, 1986

[No. 94]

Printed for the use of the
Committee on Science and Technology

ORIGINAL

U.S. GOVERNMENT PRINTING OFFICE
60-242 O
WASHINGTON : 1986

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STATUS OF THE ARTIFICIAL HEART PROGRAM

WEDNESDAY, FEBRUARY 5, 1986

House of Representatives,
Committee on Science and Technology,
Subcommittee on Investigations and Oversight,
Washington, DC.

The subcommittee met, pursuant to call, at 9:30 a.m., in room 2318, Rayburn House Office Building, Hon. Harold L. Volkmer (chairman of the subcommittee) presiding.

Mr. Volkmer. Good morning, the Subcommittee on Oversight and Investigation will come to order.

Before we begin I would like to inquire if Dr. Jack Copeland is present.

Will he acknowledge if he is present?

Does not appear to be here.

OK.

Thank you very much.

Heart disease is the leading cause of death in the United States. One approach to the treatment of heart disease is the artificial heart. From its inception in the early 1960's the artificial heart program was intended not only to save the lives of the victims of heart disease but to also allow those individuals to live healthy and productive lives in the company of their family and friends.

Largely through federally funded research the artificial heart program has advanced from a dream to a reality. It has been used as a permanent device to prolong the lives of Barney Clark, Bill Schroeder, and others.

Just recently in Minnesota an artificial heart prolonged the life of Mary Lund thereby enabling her to undergo a human heart transplant this past weekend. Through the courage of people like Barney Clark, William Schroeder, and Mary Lund we now understand more fully the potential and the problems associated with the artificial heart.

Hopefully our greater understanding will further the development of an artificial heart that will fulfill the aspirations which give birth to the artificial heart program.

There are questions that must be asked about the wisdom and utility of the present artificial heart program. Today we will examine whether the technology of the artificial heart is advanced enough to justify its usage in human beings on either a temporary or permanent basis.

We will hear about recent artificial heart implants within the last several days, under emergency conditions. And we will examine FDA procedures for handling such emergencies.

We will examine how use of an artificial heart affects the quality of life for the recipients and their families. We will review the role of the Federal Government in overseeing the development of the artificial heart and in prescribing its use.

Throughout this hearing we will be guided by the concern all America faces; the development of effective, affordable, and human means to save the lives of the victims of heart disease.

To assist us in the hearing today are two specialists most often associated with the artificial heart program, Dr. Robert Jarvik and Dr. William DeVries. We appreciate their presence and the time they have taken to be with us.

Dr. Jack Copeland was to have been here, but his presence was required at the hospital as he just this past Monday implanted yet another artificial heart. My staff was in contact just last evening, and he said he may be able to make it.

But we told him if it was necessary for him to attend his patient we would accept his statement which we have received that will be made a part of the record, and if we have any questions of him we will submit them to him in writing.

[The prepared opening statement of Mr. Volkmer follows:]

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COMMITTEE ON SCIENCE AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES
WASHINGTON, DC

HEARING ON ARTIFICIAL HEARTS

[illegible]

OPENING STATEMENT

GOOD MORNING. THE HEARING WILL COME TO ORDER.

HEART DISEASE IS THE LEADING CAUSE OF DEATH IN THE UNITED STATES. ONE APPROACH TO THE TREATMENT OF HEART DISEASE IS THE ARTIFICIAL HEART.

FROM ITS INCEPTION IN THE EARLY 1960'S, THE ARTIFICIAL HEART PROGRAM WAS INTENDED NOT ONLY TO SAVE THE LIVES OF THE VICTIMS OF HEART DISEASE, BUT ALSO TO ALLOW THOSE INDIVIDUALS TO LIVE HEALTHY AND PRODUCTIVE LIVES IN THE COMPANY OF THEIR FAMILIES AND FRIENDS. LARGELY THROUGH FEDERALLY-FUNDED RESEARCH, THE ARTIFICIAL HEART PROGRAM HAS ADVANCED FROM A DREAM TO A REALITY. IT HAS BEEN USED AS A PERMANENT DEVICE TO PROLONG THE LIVES OF BARNEY CLARK, BILL SCHROEDER AND OTHERS. JUST RECENTLY IN MINNESOTA, THE ARTIFICIAL HEART PROLONGED THE LIFE OF MARY LUND, THEREBY ENABLING HER TO UNDERGO A HUMAN HEART TRANSPLANT THIS PAST WEEKEND.

THROUGH THE COURAGE OF PEOPLE LIKE BARNEY CLARK, BILL SCHROEDER, AND MARY LUND, WE NOW UNDERSTAND MORE FULLY THE POTENTIAL AND THE PROBLEMS ASSOCIATED WITH THE ARTIFICIAL HEART. HOPEFULLY OUR GREATER UNDERSTANDING WILL FURTHER THE DEVELOPMENT OF AN ARTIFICIAL HEART THAT WILL FULFILL THE ASPIRATIONS WHICH GAVE BIRTH TO THE ARTIFICIAL HEART PROGRAM.

THERE ARE QUESTIONS THAT MUST BE ASKED ABOUT THE WISDOM AND UTILITY OF THE PRESENT ARTIFICIAL HEART PROGRAM. TODAY WE WILL EXAMINE WHETHER THE TECHNOLOGY OF THE ARTIFICIAL HEART IS ADVANCED ENOUGH TO JUSTIFY ITS USAGE IN HUMAN BEINGS ON EITHER A TEMPORARY OR PERMANENT BASIS. WE WILL HEAR ABOUT RECENT ARTIFICIAL HEART IMPLANTS WITHIN THE LAST SEVERAL DAYS, UNDER EMERGENCY CONDITIONS, AND WE WILL EXAMINE FDA'S PROCEDURES FOR HANDLING SUCH EMERGENCIES. WE WILL EXAMINE HOW USE OF AN ARTIFICIAL HEART AFFECTS THE QUALITY OF LIFE OF THE RECIPIENTS AND THEIR FAMILIES. WE WILL REVIEW THE ROLE OF THE FEDERAL GOVERNMENT IN OVERSEEING THE DEVELOPMENT OF THE ARTIFICIAL HEART AND IN PRESCRIBING ITS USE. THROUGHOUT THIS HEARING, WE WILL BE GUIDED BY A CONCERN ALL AMERICA SHARES -- THE DEVELOPMENT OF EFFECTIVE, AFFORDABLE AND HUMANE MEANS TO SAVE THE LIVES OF THE VICTIMS OF HEART DISEASE.

TO ASSIST US IN THE HEARING TODAY ARE TWO SPECIALISTS MOST OFTEN ASSOCIATED WITH THE ARTIFICIAL HEART PROGRAM -- DR. ROBERT JARVIK AND DR. WILLIAM DEVRIES. WE APPRECIATE THEIR PRESENCE AND THE TIME THEY HAVE TAKEN TO BE WITH US. DR. JACK COPELAND WAS TO HAVE BEEN HERE BUT HIS PRESENCE IS REQUIRED AT THE HOSPITAL, AS HE JUST THIS PAST MONDAY IMPLANTED YET ANOTHER ARTIFICIAL HEART. THE SUBCOMMITTEE IS ALSO PLEASED TO HAVE WITH US TODAY MEL SCHROEDER, THE SON OF ARTIFICIAL HEART RECIPIENT WILLIAM SCHROEDER.

I WILL NOW ASK THE FIRST PANEL TO BE SEATED. THE FIRST PANEL WILL BE COMPOSED OF DR. ROBERT JARVIK, THE DEVELOPER OF THE JARVIK ARTIFICIAL HEART AND PRESIDENT OF SYMBION, INC., WHICH MANUFACTURES THE JARVIK HEART; AND DR. SIDNEY WOLFE, DIRECTOR OF THE PUBLIC CITIZEN HEALTH RESEARCH GROUP.

[The prepared statement of Dr. Jack Copeland follows:]

TOTAL ARTIFICIAL HEART AS A BRIDGE TO HEART TRANSPLANTATION

Jack G. Copeland, M.D.

University of Arizona Health Sciences Center
Department of Surgery
Section of Cardiovascular and Thoracic Surgery

Tucson, Arizona 85724

Written Statement for the Hearing of the

Subcommittee on Investigations and Oversight

Committee on Science and Technology

Washington, D.C.
February 5, 1986

TOTAL ARTIFICIAL HEART AS A BRIDGE TO HEART TRANSPLANTATION

Jack G. Copeland, M.D.

In March 1985 at the University of Arizona an unauthorized total artificial heart was implanted in a young man dying of heart failure following heart transplantation. The use of this device which was called the "Phoenix Heart" attracted the large entourage of media people who had been following the total artificial heart at Louisville and perhaps over dramatized the apparent conflict with FDA regulations. Our experience with that device and the realization that the time has come for a back-up device in heart transplantation stimulated us to subsequently seek training in the implantation of the Jarvik-7 heart to acquire that heart and necessary drive mechanisms to make it function and to be ready with that device should we ever need to replace the human heart with a mechanical heart again. We were the first to be approved to use the Jarvik-7 heart as a bridge to transplant. In August of 1985 when we felt there was no other alternative but to use the Jarvik-7, we implanted that device in a young man named Michael Drummond. It supported him and allowed marked improvements of his condition over a nine day period until a donor heart was used to transplant Mr. Drummond and the Jarvik heart was removed. Michael Drummond is now alive and well at home with a transplanted heart and planning to return to work as a Safeway Assistant Manager beginning February 1986. His "bridge to transplantation" was the first successful bridge to transplantation resulting in a survivor in medical and surgical history. The following discussion outlines some of the important points relating to the Jarvik-7 heart and the Phoenix Heart as they relate to bridge to transplantation in our program.

In early March 1985 I would have been perhaps one of the last cardiothoracic surgeons in the country to espouse the use of a total artificial heart. As the Director of a successful and internationally recognized cardiac transplantation program, my concern was primarily focused on cardiac transplantation as well as the service operations of a more routine nature which we perform at the University Medical Center in Tucson. In our program of heart transplantation we had previously encountered two patients who, following heart transplantation had died on the operating room table of failure of the donor heart to function. Following the second death I had made efforts to obtain an artificial heart or a left ventricular assist device and found these were so tightly regulated that it was impossible for us to become a clinical investigator with one of these devices within a reasonable period of time. We therefore decided to apply for money from the National Institutes of Health to develop our own artificial heart, a primitive form of which had already been devised by a physician on the staff at the University Medical Center. This was turned down. We thus had no funding from the National Institutes of Health for either heart transplantation or artificial heart work when our experience with the Phoenix Heart developed.

The situation we faced when the Phoenix Heart was implanted was truly an emergency. A young man who had had a heart transplant approximately 24 hours earlier experienced a cardiac arrest early the next morning. Resuscitation was prompt, however, upon opening the man's chest and feeling his heart, it was clear that it would never beat again on its own. We were able to maintain the gentleman's pressure, neurologic function and urinary output with massage of the heart and therefore rushed him to the operating room, connected into the heart-lung machine to maintain pressure, and blood flow while we looked frantically for another donor heart. This included calling every organ procurement center in the Western United States and notifying the National Organ Transplant computer system. No hearts were available. After approximately 2 1/2 hours of time on the heart-lung machine it became clear that we would have to pronounce this gentleman dead or try a drastic therapy. I recalled that a colleague of mine in Phoenix, Arizona was working on a new device called the "Phoenix Heart". A quick call to him at approximately 5:00 a.m. revealed that such a device was available, was sterilized, and was scheduled for implantation in a calf the following day. He was willing to bring it to Tucson and have it implanted on a temporary basis while we waited for another donor heart. At that point we notified our hospital administration, our investigational review board and made plans to implant the device. The Phoenix surgeon in question, Dr. Cecil Vaughn, called the artificial heart center in Salt Lake City and informed them of our plan. They immediately flew from Salt Lake City in a Lear jet with a Jarvik-7 in hand and this, in fact, was what triggered the large following media. They, however, were much too late for our purposes and by the time they arrived we had already implanted the Phoenix heart and it was functioning. Our concern was not for regulations or the FDA, but simply to maintain the life of our patient. We spent approximately one hour explaining to his family the dilemma we faced and obtaining an informed consent. The heart did function for approximately 12 hours. We found another donor heart, and because we were uncertain as to the dependability of the Phoenix Heart, we proceeded with a second transplant. Unfortunately our patient had bacterial pneumonia and sepsis and died approximately 1 1/2 days later.

There is no other Phoenix Heart. The inventor of the Phoenix Heart, a former employee at the Texas Heart Institute where he learned his trade, is continuing to develop new models. However, his device does not differ in its basic mechanism from the Jarvik-7. To develop a "Phoenix Heart" to the same level of technology as the Jarvik-7 would take a large amount of money for engineering and mechanical development as well as a large staff and even more money for the conduct of required experiments to obtain FDA approval for clinical investigation. There is no funding for the Phoenix Heart, either at the University of Arizona or at St. Lukes Hosital in Phoenix. It, therefore, is no more than a side issue at the present time.

There is no doubt, however, that the Phoenix Heart functioned well when it was implanted in our patient. It sustained his life, improved his vital functions including blood pressure, oxygenation, kidney function and even improved his neurologic function. It is also certain that no damage resulted to the patient from the Phoenix Heart and my only regret about the entire experience is that we did not leave the Phoenix Heart in place for a much longer period of time which would have allowed the patient to recover from his cardiac arrest and perhaps allowed us to treat his infectious complications.

At this point in time we were faced with many questions and treated as experts in the field of artificial heart implantation even though our experience included only one patient and no laboratory work whatsoever. We, of course, had maintained an interest in the area of artificial devices for some time and the orientation of the Division and my own orientation were the same with regard to the theoretical role of the total artificial heart in transplantation. I felt that the bridge to transplant concept was the only realistic way in which a total artificial heart could be used in 1985. All the laboratory experiences prior to this indicated that the total artificial heart was not truly a permanent device. None of the hearts had lasted for more than a year in animals. All had failed due to clot formation, wear of the pneumatic diaphragm, infection or loss of durability of one or more valves. Further, the experience with the so-called "permanent implantation" in Utah and Louisville suggested that if the total artificial heart was in place long enough some devastating complication was bound to occur, the most likely being stroke. We thus evolved a concept of using the total artificial heart as a bridge to transplantation. The artificial heart would be used as a last resort and then for a relatively short time (1-2 weeks).

We were criticized severely by the media and various bioethicists who claimed that we should have had such a device on the shelf and available so that an unauthorized device would not have been used. Obviously this was an impossibility and in retrospect from my current perspective it is clear that unless we had had the Phoenix Heart experience we might never have had the opportunity to go on to train in the use of the Jarvik-7. The Phoenix Heart experience forced us into the artificial heart arena in one sense and provided the opportunity for us to make that transition by stimulating those around us.

We went into the Jarvik heart experience with little money, no grants, no endowments and only a great deal of enthusiasm from a small group of individuals and a very receptive institution to back us up. After training to implant the Jarvik-7 heart which included two separate trips to Salt Lake City and a total of approximately 8 operations, we devised a human subjects protocol which was approved locally by our institutional review board and a protocol which was submitted by Symbion to the FDA. This protocol was initially rejected, however, on second submission was accepted. When the case of Michael Drummond came along, we did not expect to use the Jarvik-7. However, he deteriorated very rapidly and we felt that he would not survive for more than 48 hours on medical therapy. We could not find a donor heart for him at that time and therefore we proceeded with implantation of the Jarvik-7 heart. Our impression from the experiences of others was that this implantation would be extremely difficult, that there would be tremendous amount of bleeding, renal failure would occur, hemolysis or the breakdown of red blood cells would be a major problem. None of these actually gave us any difficulty whatsoever. The amount of bleeding from the surgery was less than that normally encountered following coronary bypass. There was no renal failure, in fact the patient lost 20 kilograms or approximately 44 pounds of water of the next nine days while on the Jarvik-7 device. There was only minimal hemolysis or breakdown of red blood cells and this was never a clincially apparent problem.

On the seventh day following the implantation of the Jarvik-7 device, Mike Drummond experienced a transient neurologic deficit which was a "tiny stroke". There was no evidence on brain scanning of any damage to the brain and he has since completely recovered from this stroke which, for the most part, consisted of a stuttering and slowing of his speech. We learned a great deal from our experience with Michael Drummond. First that the device works very nicely. Second that the patient on a Jarvik-7, who has been very sick, may be expected to recover rapidly. This recovery in Mr. Drummond's case was marked by an outpouring of clotting proteins from his liver as well as the huge loss of water through his kidneys.

There were some problems with our paranoia concerning the media and we also learned from this. One was that the patient's chart each week was thinned and older parts of the chart were removed to a safe in the medical records department. This left us with only a short-term view of the patient's condition which was not satisfactory. The reason for this precaution was the fear that someone would steal his chart. A second precaution was taken with the way in which his chest x-rays were done. Some of the x-rays were digitized, making reproduction quite simple and a reproduction was made simultaneous with the original x-ray. This also was filed in a secret, locked place. We thus had routine x-rays as well as digitized x-rays to compare with each other. Having never seen the digitized x-rays before, we were at a loss to make complete sense of them and to be sure that Mr. Drummond's lungs and chest were absolutely normal.

Our final lesson from the Drummond experience was that anticoagulation is a major problem of the artificial heart, that there are many possibilities for pursuing anticoagulation and that if we had followed more closely the patient's anticoagulation status we could probably have prevented his stroke from occuring.

One would think that the visibility obtained by both of these experiences would have made it a simple matter to acquire funds to continue our research in the artificial heart area. This is far from the truth. In spite of some promising leads with private philanthropic agencies no money has come forth. Grant applications for the National Institutes of Health are in the process of being completed, however, this is a very tedious, time-consuming procedure and there is no guarantee that it will result in any reasonable amount of money which would inable us to pursue our interest in this field. Further, there is no insurance company in the United States that will fund the implantation of artificial hearts. The only institution in the United States that has pledged (by a handshake, not a contract) to do this is Humana in Louisville and I am unaware of any other hospital that has made that type of commitment.

At the University Medical Center our intention is to use the device as a temporary bridge to transplant, the hospital has indicated that they would follow our progress with these implants and would not, in the absence of adequate personal results or health insurance, charge for the period of time during which the heart is implanted, but would charge for the preoperative period as well as the post heart transplant period. We plan, therefore, to continue our experience and feel quite strongly that we have new insights into methods for anticoagulation of these patients which will enable us to be at least as successful as we were with Mike Drummond and perhaps do even better. We have no intention to use these devices for permanent implantation. However, anyone involved with the bridge to transplant program must realize and must inform his patients that if they become non-candidates for transplantation while the total artificial heart is in place that they might become de facto permanent artificial heart recipients.

Considerable changes in the design of the Jarvik-7 heart may result from our experience with Mike Drummond which has been documented in detail and is being submitted for publication at this time. Unfortunately the regulation of artificial hearts in this country will probably make it necessary to use any second or third generation of Jarvik-7 hearts in Europe or the orient since the tedious approval regulations which are also quite costly may be too much for Symbion, Inc. to handle in this country. Thus, I suspect that we will fall behind Europe in total artificial heart technology availability as we have to some extent in valvular prosthesis availability.

At the present time it would seem that the use of a total artificial heart in even a busy heart transplant program would be a rare and emergency event. It seems to me unfortunate that only a few programs in the United States and only two programs with significant numbers of transplants going on (University of Arizona and Pittsburgh) have access to the Jarvik-7 heart. It would appear that if the goal of the FDA is to slow the development of this device, they have succeeded beautifully.

One wonders if the spirit of the law as it was passed in the days following the thalidomide crisis really was to control the experimental devices which are currently under such heavy scrutiny. It would appear to me that local control of experimental technology by institutional review boards and peer review and trust in the expertise of those of us who have trained and dedicated our lives to cardiac surgery and cardiac transplantation would be a route for the government to follow. I am not sure what benefit derives from having a group of non-cardiac surgeons, non-cardiologists review the clinical indications and determine the clinical settings in which these devices are to be used. Obviously these devices are expensive, time consuming and require a disproportionate amount of effort from the investigators. However, this is no different from any other new development in the medical field.

ADDITIONAL QUESTIONS AND ANSWERS FOR THE RECORD

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE AND TECHNOLOGY
SUITE 2321 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-6371

April 7, 1986

Dr. Jack Copeland, Professor of Surgery
Arizona Health Sciences Center
1501 N. Campbell Ave.
Tucson, AZ 85724

Dear Dr. Copeland:

The Subcommittee on Investigations and Oversight appreciates your time and effort in submitting your written testimony for the February 5, 1986 hearing on artificial hearts. I regret that you could not participate in the hearing, but I fully understand the dilemma you faced, and commend you for your decision to attend your patient. Your written statement will be made a part of the record.

The Subcommittee would appreciate your written responses to the following questions:

1. Dr DeVries is working under the auspices of the Humana Corporation, which bears a majority of the costs associated with the artificial heart. Since you are at an academic institution and not a private corporation, how are the costs associated with your artificial heart program handled?

2. You have permission to use the Jarvik-7 only as a temporary device until a human heart can be found. Have you applied for permission to do permanent heart transplants with the Jarvik-7, and if not, why not?

3. Last year, you used the "Phoenix heart", an unapproved device, in a bridge-to-transplant situation. What are the basic differences between that heart and the Jarvik-7? What is the approval status of the Phoenix heart at present? Will data be submitted to FDA for future approval of this device?

4. Largely as a result of the implantation of the Phoenix heart, the FDA has promulgated guidelines which describe procedures for the emergency implant of artificial hearts. Would your use of the Phoenix heart have complied with the FDA requirements that now exist?
    - Despite the success you had with the Phoenix heart, it cannot be used again in a emergency situation until FDA approves it, and it may take several years for FDA to approve such a device. How will this affect the artificial heart program's progress?

Dr. Jack Copeland
April 7, 1986
Page 2

5. Bernadette Chayrez has now received two mini-Jarvik hearts, despite FDA's announced ban on the mini-Jarvik after its use in Mary Lund. Please explain why this was necessary and what procedures were followed to get approval for both implants.
   - Are FDA's emergency guidelines unrealistic in light of the situations you have experienced?
   - Did you get what you would regard as fully informed consent from the patient or her family? Please briefly describe the points covered in the informed consent process.

6. Given that some temporary artificial heart implants may become permanent, what guarantee is there that temporary implant patients receive the same protections and rights as patients receiving permanent implants?
   - How would you propose to balance the need for regulation to ensure maximum patient safety, and the desire of a physician to save a life in an emergency?

7. Use of the artificial heart on a temporary basis increases the number of people waiting for scarce human donor hearts. Do you have any suggestions on how to fairly allocate such a scarce resource?

8. Do you believe that the Jarvik-7 artificial heart is still an experimental device or should its use be considered an acceptable medical treatment?

9. It has been suggested that a multi-center review panel be formed to develop uniform standards related to the artificial heart implant protocol, patient selection criteria, and minimum standards for the informed consent process including forms. This panel would include, among others, representatives of the artificial heart manufacturers, the hospitals involved, and the appropriate physicians. Please comment.

Your responses to the above questions should be submitted by April 24, 1986 to:

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex I
Washington, DC 20515-6307

I want to extend my thanks for your service to the Subcommittee.

Sincerely,

Harold L. Volkmer
Chairman
Subcommittee on Investigations
and Oversight

The University of Arizona

Health Sciences Center
College of Medicine
Department of Surgery
Section of Cardiovascular and
Thoracic Surgery
Tucson, Arizona 85724
(602) 626-6339

April 21, 1986

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex I
Washington, DC 20515-6307

Dear Dr. Glowinski:

Thank you for allowing me to answer your questions. I will answer them in the order asked.

1. The cost of our artificial heart program at the University Medical Center in Tucson are handled as follows. Capital investments in drivers, artificial hearts, a mock-circulation, and the hiring of various engineering personnel (3), has been jointly shared by the College of Medicine and the hospital. Costs for the implants have been covered by the patients and their insurance companies. There have been some failures to pay, and these have been written off by the hospital.

2. At present I am not interested in a permanent implantation of the Jarvik-7 or any other artificial heart. Perhaps once we obtain a portable drive unit (Heimes driver), I will be more interested. And certainly, when total implantability is achieved, either with a ventricular assist device or a total artificial heart, the appeal for long-term implantation will be great. In the meantime it seems to me that the transplantation setting is the best one in which to test the total artificial heart in 1986.

3. The so-called "Phoenix heart" differs in size and shape from the Jarvik heart. The current version is smaller than even the mini-Jarvik, however has a stroke volume of approximately 100cc. The compactness is obtained by changing the shape of the device making it more elongated. The inlet and outlet valves of the Phoenix heart at present are St. Jude valves of 29mm and 27mm respectively, the same size, but a different make from those used in the Jarvik-7 (Medtronic Hall). The diaphragm in the Phoenix heart is tethered so that it takes on the shape of a cone or tent that is inflated and deflated. The

segmented polyurethane membrane is only single thickness. This device has had very limited testing, has not been subjected to any FDA protocols, and is first being bench tested for hemodynamic and durability considerations. At some point in the future data may be submitted to the FDA for approval of this heart. I suspect this will take some time, but I am impressed with the promise of the Phoenix heart for the future.

4. The Institutional Review Board guidelines do provide for use by a physician of any device in a life threatening emergency that he feels may save his patient's life. These guidelines were written well in advance of our experience with the Phoenix heart. I believe if we were to use the Phoenix heart or a similar but unapproved device that they would fall under current FDA guildelines, but that special communication with the FDA would not only be warranted but wise. Obviously the regulatory role of the FDA restricts in many ways the development of artificial hearts. While the FDA views itself as stimulating good science and good research, given the current financial constraints on most research programs and small businesses involved in artificial heart technology, this type of restriction is at times overwhelming. I suspect that there would not be nearly as great a problem if the total artificial heart had a lower profile, but unfortunately news of the total artificial heart sells newspapers.

5. In the case of Bernadette Chayrez, the FDA was consulted daily for approximately five days in a row with regard to the initial mini-Jarvik implant. They repeatedly gave their approval for our use of this mini-Jarvik in the first case. After Mrs. Chayrez's rejection and emergency reimplant, we also talked with the FDA extensively. Currently the experience with Mary Lund and Mrs. Chayrez is being used in lieu of further animal experimentation as proof of the chronic function of the device. The FDA has accepted this experience pending data submission.

   I feel the FDA guidelines are perhaps too stringent in the case of the mini-Jarvik which is definitely an efficacious device and has supported Bernadette Chayrez now for more than 60 days without any evidence of thromboembolism or device failure. Hemolysis has been minimal, and the problems we have faced have been largely those created by rejection and infection.

I believe we obtained as fully an informed consent as we possibly could have from Mrs. Chayrez and her family. I have enclosed a copy of the consent form used. In addition to the consent form, a question and answer session with the patient and her mother was recorded and transcribed which covered the key points regarding what to do if a massive stroke occurred after implantation. It was decided by the patient and her mother that in this event they would both want the machine turned off. Informed consent seems to be a major issue in the eyes of the highly educated, sophisticated, and medically aware bioethicists. Unfortunately most lay people are completely lost after about five minutes of informed consent discussion. Perhaps informed consent should be carried out as a classroom procedure with multiple sessions and teaching. However, time is not always available and a weighing of all of the points by the patient is impossible since he has so little understanding for the great complexity of the field in which we are dealing. I think you will see our informed consent covers all of the major catastrophies which could occur. Obviously this is discouraging to the patient and the family, but all of these points are stressed very carefully, and in fact in most cases we have read the consent in its entirety aloud to the patient and explained it word by word and paragraph by paragraph if necessary. I believe we have done everything we can do to fully inform our patients short of restricting the procedure to recipients who have a full medical education.

6. There is no guarantee that the patient or his family are going to understand anything we say about informed consent or the procedure. In fact there is no such thing as a guarantee in any of the biological sciences in medicine or in surgery. I think a consent form such as we have submitted, plus an honest discussion of the prospects with the total artificial heart and of the possible catastrophies and of possible alternatives in face of catastrophy is all we can do to ensure that our patient and his family are prepared.

7. I don't believe that use of the artificial heart on a temporary basis increases the number of people waiting for scarce human donor hearts. On the contrary. If the total artificial heart is used only in those candidates for heart transplantation who have been preselected or in patients who have already had transplants, it does not increase the number. Further, it has been well documented by numerous papers in the literature and

anecdotal information from programs around the world that from 20% to 40% of patients die while they are waiting for a transplant after having been chosen as an active transplant candidate. This makes the waiting period for transplantation the highest mortality in the first year after patient selection. Higher in fact than the mortality rate expected after transplantation. Another point which is important and should be stressed, is that placement of a total heart in a patient reduces the urgency for transplantation by making him hemodynamically stable. If we have learned anything from our three patients, it is that we should not allow any circumstance to force us into transplantation until the patient's condition is absolutely perfect for transplantation. If the artificial heart is put into patients who are not transplant candidates now with the hope of making them transplant candidates, then your point would be correct. But to the best of my knowledge, this is not being done anywhere in the United States or the world.

8. I still believe the Jarvik-7 artificial heart is an experimental device and should be treated as such until we have more data. In the history of the world there have only been about 17 or 18 total artificial heart implants as bridge to transplantation. Among these there have been less than a dozen Jarvik-7 hearts implanted. This does not constitute a sufficient data base to remove the device from its experimental status.

9. Recently all of the principal investigators involved with the Jarvik-7 heart met in Salt Lake City to discuss their experiences. At the present time there is no consensus on artificial heart implant protocols, patient selection criteria, minimum standards for the informed consent process, treatment with anticoagulation therapy, indications for going on to transplantation, laboratory data to be obtained in all patient cases, infectious disease monitoring protocols, etc. Some of these items, such as a minimum standard for informed consent could possibly be put together by a committee. However there are many unknowns which we will have to learn from experience such as the best anticoagulation protocol, indications for implantation, and indications for transplantation after implantation. Perhaps such a panel of people could decide which issues would be able to be addressed by a committee and acceptable to all investigators and which issues are best left to the investigators for the moment until a consensus is developed from experimentation. To control the experiment too much at the present time may deny us from obtaining important information. I believe that committee directed, goal-oriented research is beneficial but if one looks

at the history of significant developments in medicine, one finds that they usually come from the individual struggle and toil of people who are very dedicated, are searching for an answer, and are receptive to many forms of information. I do not believe the committee context is the best for obtaining information, nor do I believe that goal-oriented research such as is currently in vogue at the NIH ever does what it sets out to do.

Sincerely,

Copeland

Jack G. Copeland, M.D.
Professor and Chief

JGC/tle

Enclosures

Authorization for and Consent to Implantation of the Symbion Total Artificial Heart

Purpose: To prolong human life in patients with terminal heart disease.

You have been selected for implantation of an artificial heart (1) because you have end stage heart disease for which there is no further medical or surgical treatment available; or (2) because you are experiencing failure of your transplanted heart; and (3) at this time, your physical condition is satisfactory enough to withstand the implant procedure. You are being asked to give consent to the above titled procedure. The purpose of this procedure is to implant a temporary Symbion total artificial heart until a suitable donor heart is available for transplantation and you are felt to be an appropriate surgical candidate for transplantation. The artificial heart proposed for use in your care is an experimental device not yet approved by the FDA for routine use and as such its implantation constitutes research. The purpose of this research is to study the possiblity that an artificial heart can prolong life in patients with terminal heart disease until cardiac transplantation can be performed. We estimate that 5 to 10 patients a year will recieve an artificial heart as part of this project at the University of Arizona Health Sciences Center, and this project will continue for a period of approximately five years. The artificial heart will be implanted only after all treatment alternatives have been exhausted, including medications which can improve the function of your own heart and maintain your blood pressure, use of an intra aortic balloon pump, or insertion of a left ventricualr assist device (LVAD). The LVAD is also an experimental device which has been approved for use in certain medical centers. The intraaortic ballon pump and the LVAD do not require removal of your own heart and are designed for use in patients who have a poorly functioning left ventricle, but an adequate right ventricle. These alternatives will be thoroughly discussed with you and/or your family.

The purpose of the artificial heart is to maintain life until a suitable donor heart is found. Finding this donor heart may require a few days to a few months; the average waiting time for transplant recipients in our center is 36 days, with the longest wait in the last year being 3 months. The artificial heart will be implanted with the intention of use ranging from several days up to three months. While it is possible that cardiac transplantation could not be performed within three months, due to lack of a donor heart, or due to reversible medical complications such as pulmonary edema (fluid in the lungs), or ongoing infection, it is unlikely. Should this occur, the artificial heart will remain in place as long as needed, and your hospital stay will be extended. If you develop irreversible complications such as renal failure, a massive stroke or infection which cannot be resolved by medical or surgical therapy, it is possible that you would no longer be a candidate for cardiac transplantation. If this were to occur, you would be supported by the artificial heart as long as possible.

Explanation of Procedure

1. Artificial heart implantation

   The Symbion total artificial heart has been tested extensively in the laboratory and has been successfully implanted in 5 patients. In animals, the longest implant has survived 260 days, while in humans one patient continues to survive after 170 days. The implantation procedure takes two to three hours and is performed while the patient is on the heart-lung machine. It will require the removal of the right and left ventricles of the your natural heart. The Symbion heart will then be placed in the your chest and attached to the right and left atrium, aorta and pulmonary artery of the natural heart. The surgery itself will be performed by members of the cardiac transplant team. The Symbion heart is attached to two tubes which pass through the skin and connect to a portable external drive console which powers the heart with compressed air. You will remain in the hospital until it is possible to replace the artificial heart with a compatible human donor heart.

2. Other procedures

   Blood tests, removing approximately one ounce of blood, 4 times per day for 3 days and then daily.
   Administration of antibiotics to prevent infection at the time of surgery.
   Administration of coumadin, a medication to prevent formation of blood clots.
   Administration of lasix, a medication to reduce any excess fluid in the body.

3. Post Operative Recovery Period

   While awaiting a donor heart, you will remain in the hospital, attached to the external drive console of the artificial heart. You will undergo daily physical exams and laboratory procedures. You may need medications to help control your blood pressure and diuretics to control your fluid levels. In addition, you will be taking coumadin, a blood thinner, which can cause excessive bleeding. (However, you will be carefully monitored with blood tests while on this medication.) If an infection develops, you will be placed on antibiotics. As soon as you are medically stable, you will be placed on an oral diet and will have I.V.'s only as needed.

4. Risks of the Procedure

a) Bleeding from the operative procedures, possibly necessitating further surgery.
b) Thromboembolism or blood clots which can form and travel to other parts of the body and could possibly cause a stroke or seizure activity.
c) Infection in the skin, the chest or the mechanical heart valves.
d) Mechanical failure of the artificial heart or one of its components.
e) Severe anxiety reaction or psychosis; these are unlikely, but possible.
f) If you weigh less than 150 pounds, it may be difficult or impossible to close the sternum after implantation of the artificial heart. However, the skin will be closed.

5. Cost of the Procedure

All costs of the procedure, hospital care, and subsequent follow up shall be borne by you and/or your insurance company. The expected cost of the implantation and subsequent human heart transplantation is approximately $80,000, which includes about $54,000 in hospitalization and $26,000 for surgery, anesthesia, radiology, pathology, consultants and the cost of the mechanical heart. Your insurance company may not not cover these costs.

The Symbion total artificial heart is an investigational device designed to prolong life until cardiac transplantation is possible.There is no guarantee as to the result of the surgery or the performance of the device itself. Confidentiality of the patient will be maintained at all times and the identity of the patient will be revealed to the public only with the prior consent of the patient or his family. However, we can not guarentee that the press will not discover that a transplant is being performed. In addition, the Food and Drug Administration may examine records of the device's use at any time.

Adverse reactions are a possibility in any research program despite the use of high standards of care and could occur without negligence attributable to either the subject or the investigator involved. Reactions which can be foreseen have been described in this consent form. However, unforseeable injury may also occur and may require care. Financial compensation for research related injury or for wages or time lost is not available. Further information is available from Dr. Jack Copeland.

I have read this subject's consent form. The nature, demands, risks, and benefits of the project have been explained to me. I understand that I may ask questions and that I am free to withdraw from the project at any time without incurring ill will or affecting my medical care. I also understand that this consent form will be filed in an area designated by the Human Subjects Committee with access restricted to the principal investigator or authorized representatives of the particular department. A copy of this consent form will be given to me.

X Bernadette Chavez 1/29/86
Subject's Signature Date

Tillie S Chavez 1/29/86
Parent/Guardian Signature (if necessary) Date

I have carefully explained to the subject the nature of the above project. I hereby certify that to the best of my knowledge the subject who is signing this consent form understands clearly the nature, demands, benefits, and risks involved in his/her participation. A medical problem or language or educational barrier has not precluded this understanding.

Investigator's Signature Date

THE UNIVERSITY OF ARIZONA
TUCSON, ARIZONA 85724

UNIVERSITY HOSPITAL

TIM: This is Tim Icenogle recording events of 2/2/86. The time is 6:37 p.m., and with me is Bernadette Chayrez, Tillie Chayrez, and Annie Nicholson. Do you understand that this conversation is being recorded, Bernadette?

BERNADETTE: Yes, sir.

TIM: Bernadette, are you in control of your mental functions; that is, are you alert and can you think clearly?

BERNADETTE: Yes, I can.

TIM: Right now you are being considered for an artificial heart implantation to treat you for congestive heart failure. Do you understand this?

BERNADETTE: Yes.

TIM: Have the risks and the complications of implantation of the total artificial heart been explained?

BERNADETTE: Yes - very clear.

TIM: Okay. Now, Bernadette, should there be a stroke or brain damage following implantation of the artificial heart, what would you want your family to do?

BERNADETTE: Turn the machine off.

TIM: Okay. Tillie, are you in agreement with Bernadette's wishes?

TILLIE: Yes.

TIM: Okay.

TIM: Bernadette, do you have any wishes that you'd like to have conveyed?

BERNADETTE: I want the insurance I have at Motorola for $50,000 left for my parents to take care of my kids.

TIM: Do you want your children to go with your parents?

BERNADETTE: Yes...

TIM: Okay.

BERNADETTE: ...always.

TIM: Did you say always?

BERNADETTE: Yes.

Continued next page . . .

TIM: All right. Thank you very much. Do you have any further comments?

BERNADETTE: No.

TIM: Tillie Chayrez, do you have any further comments?

TILLIE: No.

TIM: Okay, thank you very much.

Timothy B. Icenogle MD
Timothy B. Icenogle, M.D.
Instructor, Surgery

Bernadette Chayrez
Bernadette Chayrez

Tillie S. Chayrez
Tillie Chayrez

Annie Nicholson RN
Annie Nicholson

Mr. **Volkmer**. I will now ask the first panel to be seated.

The first panel will be composed of Dr. Robert Jarvik, the developer of the Jarvik artificial heart and president of Symbion, Inc., which manufactures the Jarvik heart.

And Dr. Sydney Wolfe, director of Public Citizen Health Research Group.

And before we start with our testimony, I would like to recognize the ranking minority member, the gentleman from California, Mr. Packard, for any statement he would like to make.

Mr. **Packard**. Thank you.

Thank you, Mr. Chairman.

I believe that we have made tremendous strides in heart and artificial—or in human and artificial heart implantations. And I commend the researchers, the physicians, and the patients who have allowed this progress to take place.

The need for an artificial heart, either temporary or permanent, is clearly justified by the simple reality that heart disease is the leading cause of death in this country.

Prominent researchers and those concerned with the ethics are raising serious questions about clinical trials and the direction of artificial heart research. I am pleased that we are examining these legitimate concerns, which include medical complications, the quality of life for artificial heart patients, and oversight by the Food and Drug Administration.

We must be careful, however, to not unduly hinder the advance of research. A balance certainly must be reached.

I welcome expert opinion on the current state of artificial heart research and how we can promote continued progress in an ethical and medically responsible manner.

Thank you, Mr. Chairman.

Mr. **Volkmer**. I thank the gentleman from California.

With that I will first mention for the record, Dr. Jarvik, do you have someone with you today at the table?

Dr. **Jarvik**. Yes.

Mr. **Volkmer**. Would you identify him for the record so we can have——

Dr. **Jarvik**. Yes. This is Mr. Don Grabarz, who is vice president for regulatory affairs for Symbion.

Mr. **Volkmer**. Fine.

At this time you may proceed, Dr. Jarvik, with your statement.

STATEMENTS OF DR. ROBERT K. JARVIK, PRESIDENT, SYMBION, INC., SALT LAKE CITY, UT, ACCOMPANIED BY DR. DON GRABARZ; AND DR. SIDNEY M. WOLFE, DIRECTOR, PUBLIC CITIZEN HEALTH RESEARCH GROUP, WASHINGTON, DC

Mr. **Volkmer**. I would like to point out that all the statements of all the witnesses will be incorporated in the record in full. And you may either read the statement in full or you may either summarize.

Dr. Jarvik.

Dr. **Jarvik**. Thank you.

Chairman Volkmer, committee members, guests, there is a common reason that we are here today. We have in this country a belief in science and technology as a foundation of our heritage and as a cornerstone of our future.

And we have a dedication to preserve and expand our freedom and to apply our recognition of the value of each human life to improve our society. The challenge is to bring warmth to science, and to apply technology in line with our human values, and the challenge is to combine them to bring them together.

Nowhere is this more apparent than with the artificial heart. And no time in our history has it been more apparent that Americans care about the human side of our scientific efforts.

At NASA's request I served as a judge in the Teacher-in-Space Program in the selection of the 10 finalists. I first met Christa McAuliffe at the White House.

I ranked her 10½ on a final selection scale above any other candidate. I voted for her, and I was delighted when she was chosen.

And last week when she died, my thoughts turned to Mary Lund, another young woman on the brink of it all living with the Jarvik-7 heart, hoping that they will find her a transplant.

Christa's death was one of a series of events that I felt very personally. From the selfless willingness to enter the unknown, that men such as Barney Clark and Bill Schroeder have shown, to the elation that others with the artificial heart have felt, those who have truly done well, Leif Stenberg, Michael Drummond, Thomas Gaidosh.

Michael recently wrote these simple words to me, "Best of luck in your future with the device that saved my life."

That says it all.

We are here today because the artificial heart can make a difference. And because there are few frontiers as clear as space. This is one of them.

But mostly because there is an overwhelming medical need. Heart disease kills a million Americans each year. As many as all other diseases combined.

Heart disease will kill 500 people today as we hold these hearings. Another 500 tomorrow morning. And on, and on.

The public cares intensely about medical progress in this field. Artificial heart has our attention.

It has become a symbolic focus of many efforts to approach the problem through medical science and technology. But also it may provide a model of positivism that America can well use.

We do not pretend that the artificial heart is the sole answer. But it is becoming part of the answer.

Heart disease will only be markedly reduced through a combination of efforts, including advances in drugs, new methods such as coronary angioplasty, and above all, preventive medicine.

There is no doubt of the devastating effects of smoking, obesity, and hypertension. I speak in favor of prevention at every opportunity.

I support legislation to eliminate all cigarette advertising. I don't smoke, I exercise regularly, and I am only 7 percent body fat. Something less than obese.

I can't say I live a life entirely free of stress. Editorials such as a recent one in the New York Times entitled, "The Heart that Fizzled," sometimes send my blood pressure through the roof.

But after 15 years of work on this program, I have become convinced that artificial hearts will be practical; will provide a high quality of life for tens of thousands of Americans; and will be cost effective.

We face many challenges but I am sure we will succeed for these reasons: Artificial heart technology is fundamentally sound. It works. It has been developed through decades of intensive research, the heart-lung machine, the intra-aortic balloon pump, the left heart assist device, the total artificial heart.

These all share common elements of blood pumping technology successfully applied in hundreds of thousands of patients each year. Technology in biomaterials, vascular grafts and prosthetic heart valves is advanced. Techniques in cardiac surgery and postoperative care are well developed.

And perhaps, most importantly, many hundreds of talented and dedicated specialists in medicine, engineering, and numerous related fields are willing to continue to work hard to make the artificial heart program succeed.

The American public wants success. And the goal is undisputed. A high quality of life available to all our citizens at a reasonable cost. We know what we are working to accomplish.

I have frequently been referred to as the inventor of the artificial heart; I am not, although I have invented some crucial elements of the system.

The basic functional concept dates back to the work of Kolff, Akutsu, DeBakey, Liotta, Kwan-Gett, and others who contributed the evolution of this type of blood pump in the late fifties and the decade of the sixties. We have learned that a very simple pumping mechanism can effectively replace the natural heart and that human patients can be sustained with excellent hemodynamic function for more than a year.

Perhaps my major technological contribution has been the development of the multilayered-graphite lubricated polyurethane diaphragm which must flex 40 million cycles a year, (that is 40 million heart beats) and routinely lasts 4 to 5 years in Jarvik-7 hearts tested on the mock circulation. Previous polyurethane diaphragms broke within a month.

I believe we will further improve the design and that highly reliable hearts will pump 8 to 10 years without a failure.

Animal research with the Jarvik-7 heart and its predecessors was funded by the National Institutes of Health for many years. With this support Dr. Don Olsen and his team at the University of Utah, made major contributions in surgical techniques postoperative care, and physiological evaluation. NIH is also supporting many other related programs and there is extensive scientific literature in the field.

I believe that the level of NIH funding presently planned for the artificial heart over the next several years represents inadequate follow-through on the $200 million Government investment in this technology to date. A greatly expanded program, including clinical evaluations of pneumatic systems as a step toward the development of more desirable electric systems, and would help the United States retain the leadership which it now holds.

The decision to begin human studies with the Jarvik-7 heart was based on our substantiated belief that we could offer real hope of an extended and improved life to patients who otherwise faced certain death, and that we could gain important scientific knowledge.

Barney Clark saw the animals with artificial hearts 6 weeks before his surgery. He understood what to expect and had time to think about it. His consent was thoroughly informed.

The protocol for this first case took more than 2 years to develop and approve. Ethical considerations were paramount.

Bear in mind that the basic indication for use of the artificial heart remains unchanged today. The patient must face imminent death, when no other medical treatment is judged to have a reasonable chance of success, an informed consent must be granted by the patient or a responsible family member.

The artificial heart is not implanted in any patient who is a transplant candidate and can wait any longer for a donor organ. Only when waiting for a donor is no longer possible can the artificial heart be used.

To date six such cases have been done with the Jarvik heart. Two of the patients are at home and in excellent condition after the artificial heart was removed and the transplant performed.

The third, Mary Lund, received a transplant 3 days after the shuttle disaster and is now doing very well. Over the past 3 days three other patients have received the Jarvik-7 heart as a bridge-to-transplant; a 39-year old man operated by Dr. Griffith, in Pittsburgh; a 40-year old woman operated by Dr. Copeland, in Tucson; and a 41-year-old man operated by Dr. Frazier and Dr. Cooley in Houston. All three patients are stable, making progress, and will hopefully receive transplants within a few weeks.

We have had five cases of permanent use. Bill Schroeder is alive 14 months after the implant. For a time he was in far better condition than Barney Clark. He has lived in an apartment near the hospital, and has revisited his home in Jasper, IN. But he has been severely handicapped by the effects of his strokes, and my respect for his courage and fortitude is ever increasing.

His family, as well as Dr. DeVries and the Humana team, have retained their deep commitment to him through such difficult times. It is a story of both triumph and tragedy.

Murray Haydon has been living almost 1 year with his implant. Five months after surgery he suffered a stroke from which he completely recovered in a few days. He is neurologically normal with no evidence of thromboembolism.

He has had continuing problems with lung function due to a post surgical bleeding problem when a monitoring catheter was removed. This has nothing to do with the heart itself.

Leif Stenberg survived 7½ months. He was in dismal condition at the time of the implant. He regained strength and he frequently left the hospital with a portable drive system. He visited friends, went out to restaurants, and even walked up five flights of stairs to attend a birthday party at his son's apartment.

He ultimately died following a severe brain hemorrhage, related to infection and thromboembolism.

Jack Burcham died 10 days after surgery from bleeding, related in part to poor fit of the heart in his chest. He had a deformity of his rib cage which made fit difficult and we did not have a small size heart available as a backup.

Thus, of the 11 patients, 8 are alive today. The average survival of the permanent use patients is about 7½ months. Their life expectancy without it was a matter of hours or days. We have demonstrated that a high quality of life is possible.

We have learned a great deal about the medical management of these patients. We have had few equipment problems, and no catastrophic device failures.

We well understand the areas in the heart itself that are susceptible to thrombus formation if anticoagulation is not adequate. We have tested designs in animals which are a significant improvements and are in the process of finalizing a design modifications which I strongly believe will greatly reduce the risk of stroke.

So far, we have evidence that the artificial heart is free of calcification in humans. This has been a severe problem in calves.

I believe future work, both with bridge to transplant and permanent use, is appropriate. There are a wide range of scientific questions of inherent interest which cannot be answered without many, many more human cases.

Symbion has trained nine teams in the United States, and four abroad to implant the heart. The principal investigtors include, Dr. DeVries, Dr. Copeland, Dr. Joyce, Dr. Griffith, and Dr. Semb, all of whom successfully implanted the heart in their patients.

Others soon will begin. Dr. Frazier and Dr. Cooley, have just begun, including Dr. Noon, and Dr. DeBakey, Dr. Gay, Dr. Tector, and Dr. Vaughn.

Abroad, some leading transplant experts including Dr. English in Cambridge, England; Dr. Cabrol in Paris, France; and Dr. Koen, in Ottawa, Canada have completed their training.

The extensive knowledge of these physicians and the commitment of their institutions speaks highly of the confidence the medical community has that human application of the Jarvik-7 heart is worthwhile.

It is revealing to consider the history of other new innovations in medicine. Heart transplant now achieves 70 to 80 percent 1-year survival with an excellent quality of life. It was not always so.

Of the first 50 patients to undergo human heart transplants, eight died from thromboembolism or stroke. That is 16 percent.

With the first eight Jarvik-7 heart patients, because I can't count the last three, which are so recent, of the first eight, one died from the complications related to thromboembolism or stroke. That is 12½ percent.

Of the transplant patients, nine died of heart failure and four from infection. Of the artificial heart patients, nine have died of heart failure, two have died from infection.

Most of the early problems with the transplants are the same problems we are working to overcome, but the public doesn't realize that they are less severe with the artificial heart than with the initial use of transplant.

Of the first 50 transplant patients, 21 died in less than a week, that is 42 percent. None of our artificial heart patients have died in less than a week. With the initial transplant group, 11 survived more than 6 months. That is 22 percent.

With the permanent total heart, three of five have survived more than 6 months. That is 60 percent, about three times as many long term survivors as with transplant.

Had the early results with transplant been as good as our initial artificial heart results, transplant may have become more widely applied faster.

It is also important to note that although the FDA was not involved, transplant did not become widespread until the medical community and the public felt that the results warranted it.

The first 15 patients treated with artificial kidneys died within days, but 250,000 people are now sustained with dialysis for many years of worthwhile life.

The first cardiac pacemakers were the size of a television set and were wheeled around with the patient on a cart. They are now about the size of a stack of three or four silver dollars. They last reliably for more than 10 years.

There are countless other examples.

We face serious problems regarding Federal review and regulation of the artificial heart. Symbion has made every effort to cooperate effectively with the FDA.

Since 1980 we have maintained an extensive correspondence with us the FDA which now includes over 2,600 pages of documents. FDA officials have visited Symbion and participated with us in several forums dealing with the issues, including a major conference Symbion sponsored on the artificial heart and public policy.

We have frequently visited FDA officials in Washington. Commissioner Young has taken an active personal interest in the program—especially the emergency use guidelines.

Artificial heart need not require so much attention from the FDA. Dr. Dwight Harken, clinical professor of surgery (emeritus), of Harvard Medical School has said: "A device is safe when it's safer than the disease it treats and is the best available."

I believe that in appropriate circumstances the artificial heart is far safer than any other available treatment. I believe the FDA is having difficulty because the law requires them to assess risk/benefit ratio and judge quality of life. In my view, a risk is acceptable when the person at risk understands and accepts it.

Very simple.

Regarding quality of life; I believe FDA has no choice but to decide that life is always preferable to death.

My personal belief is that there are many things worse than death and that prolonging suffering is one of them. That is not what the artificial heart does, and if it were, I would not continue to work with it.

But the decision is subjective—of when the risk of a possible complication is so high that a patient should not be allowed the choice and the law would thereby mandate his or her death. That decision should not be a matter of law, it should remain between the patient and the physician.

I believe that the Medical Devices Act of 1976 is right to require informed consent to the fullest extent practical.

Patients cannot understand everything and an essential element must be trust in the physician's judgment. The law must not interfere with the basic doctor/patient relationship of trust and commitment—long accepted as the basis of medical ethics, and so well expressed 2,000 years ago in the Oath of Hippocrates.

The 1976 Medical Devices Act provided a mechanism called the investigational device exemption which was intended to facilitate the introduction of important new advances. A large portion of the responsibility for review was placed on the local institutional review boards.

I believe Congress was wise in that decision and it should not be changed.

Symbion has taken a clear position regarding emergency use of life saving methods and devices. That is, that after the institutional review board has approved use, the device should be available for use in an emergency—even though the FDA may not have had time to complete its review. Physicians and teams which may have made the effort to prepare and obtain IRB approval are placed in an untenable position that they must deny the use of a new technology they believe in to their own patients, who may be dying before their very eyes.

Figuratively, we cannot invent life jackets and then prohibit their use until we evaluate the straps and buckles and decide whether they should be yellow or orange. The law should recognize responsibility for denial of lifesaving technology as well as the need to insure and maximize the safety of medical devices. We need to wisely balance these two responsibilities.

I hope Congress will help relieve some of the pressure FDA is under because of the extensive publicity of the artificial heart. Usually an investigational device exemption permits testing in several hundred or even a thousand patients prior to premarket approval.

I believe it is proven without a doubt, that the Jarvik-7 heart does save lives, and that there is now enough data for the FDA to treat it in the same way other new devices are handled. I believe it is appropriate to approve additional institutions to study the artificial heart.

I believe the review of the results of these studies need not be more strenuous than with other new lifesaving medical devices. Yet to date, I believe it has been more strenuous. The increased reporting requirements that Dr. DeVries faces following review of his program by the FDA advisory panel, and the restriction to no more than one patient every 3 months, in my view, mandates delay.

Dr. David Skinner, chairman of surgery at the University of Chicago, has said, "The only question remaining about the artificial heart is whether it will be an import or an export."

The denial of approval to use the Jarvik-7 heart as a permanent device at other institutions until Dr. DeVries completes his series of seven cases is forcing us to take the program abroad. We have many excellent medical scientists in this country who have the commitment and the resources to be world leaders, if our Government would trust them and encourage them.

Finally, I would like to briefly address an issue of economics. I am president of Symbion, Inc., a small publicly held company, and acutely recognize that new technologies spawned by government financed university research can only become of widespread benefit to the public if they can be produced profitably. I believe our future benefits from entrepreneurial success.

I believe in free enterprise. I believe our future benefits from entrepreneurial success. I recognize in the artificial heart two things:

One, that it will only be broadly applied when its success and value is inherently obvious to the public. Until it works very well indeed, it will consume an insignificant portion of our national resources.

And two, unless our system, supported by Government, not impeded, can move quickly enough, then free enterprise, especially through small business, cannot succeed with major advances such as this.

Symbion has invested heavily in research and development. Our losses attributable to the artificial heart side of our business are about $500,000 for each human case done so far.

I would hope that Congress could help: By affirming that it is in the public interest to achieve an excellent value-effective artificial heart sooner rather than later; by affirming that world leadership in science is an American goal, and artificial heart is part of it; by recognizing the educational impact of our work and the interest we are generating among the Nation's youth; and by affirming again that the application of science and technology to the benefit of humanity is, indeed, one thing Americans do well.

Thank you.

[Additional questions and answers, plus the prepared statement of Dr. Robert K. Jarvik follow:]

ADDITIONAL QUESTIONS AND ANSWERS FOR THE RECORD

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Executive Director

ROBERT C KETCHAM
General Counsel

JOYCE GROSS FREIWALD
Republican Staff Director

April 7, 1986

Dr. Robert K. Jarvik, President
Symbion, Inc.
825 North 300 West
Salt Lake City, UT 84103

Dear Dr. Jarvik:

Enclosed is a copy of the transcript from the February 5, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight about artificial hearts. Attached to the transcript are instructions for submitting requests for changes or clarifications. Please review these instructions and the enclosed transcript of your remarks carefully.

The Subcommittee would also appreciate your written responses to the following questions:

1. One of the concerns sometimes raised about use of the artificial heart is that use of the artificial heart will cause a shift in priorities among heart transplant patients. Please comment.

2. You stated during the hearing that the artificial heart is used only in lifesaving situations. In view of this, do you believe FDA's draft emergency use policy should apply to the artificial heart or do you believe changes are necessary in the draft policy?

3. Based on your experience with the permanent implants of the Jarvik-7 performed to date, how do you plan to modify the implant protocols for future implants approved by FDA?
    - Will these changes in the implant protocols necessitate added review by the FDA?

4. I understand that all the data collected concerning the function of the artificial heart patients is considered by FDA to be confidential information. Given the high level of visibility which both these surgical procedures and the patients involved have received, what purpose is served by keeping this information from medical professionals - particularly when many surgeons have performed similar surgical transplants?

5. At present, Dr. DeVries is the only physician approved to implant the Jarvik-7 heart on a permanent basis. Is Symbion planning to apply for similar permission for any other investigators? If not, why?
6. It has been suggested that a multi-center review panel be formed to develop uniform standards related to the artificial heart implant protocol, patient selection criteria and minimum standards for the informed consent process, including forms. This panel would include, among others, representatives of the artificial heart manufacturers, the hospitals involved, and the appropriate physicians. Please comment.

Your copy of the transcript, together with any written requests for changes, and your responses to the above questions should be returned by April 24, 1986 to:

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex I
Washington, DC 20515-6307

Your testimony at the hearing was extremely valuable to the Members, and I want to extend our thanks for your participation and service to the Subcommittee.

Sincerely,

Harold L. Volkmer
Chairman
Subcommittee on Investigations
and Oversight

HLV/Gmbh

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. symbion, inc.

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May 12, 1986

Mr. Harold L. Volkmer, Chairman
Committee on Investigations and Oversight
U.S. House Of Representatives
Suite 2321 Rayburn House Office Building
Washington, DC 20515

Dear Congressman Volkmer:

I apologize for my late response to your follow-up questions after the February 5 hearing. I have been out of town practically all of the month of April and have only recently had the opportunity to give your excellent questions the thoughtful consideration they deserve.

First let me express my sincere appreciation of the thorough and professional manner in which the hearing was planned, researched, arranged, and conducted. I know it is your job to do a good job of that and I believe it was apparent to us all that the hearing was very well run.

Let me now respond to your questions.

Question: 1. One of the concerns sometimes raised about use of the artificial heart is that use of the artificial heart will cause a shift in priorities among heart transplant patients. Please comment.

Response: There are a number of specific possible considerations about the hypothetical shift in priorities among heart transplant patients which might occur if the artificial heart as bridge-to-transplant is more widely used. To be more specific rather than using the word "concerns," I will refer to the terms potential problems and also potential benefits, since both these are "concerns." A potential problem is that patients who are awaiting transplant while maintained on artificial hearts will "move to the front of the line" and obtain preferential access to scarce donor organs. This problem would be especially serious in the event that there was a higher failure rate in the organs so utilized and, therefore, effectively, there was waste of the donor hearts. This is clearly not occurring. To date, there have been twelve patients implanted with the JARVIK-7® heart as a bridge-to-transplant. Of these twelve patients, two died on the artificial heart, both from infections unrelated to the device. During most of the time that both of these individuals were supported with the heart, they were not on the recipient list for a heart transplant because their condition was not sufficiently good to expect a reasonable chance of success if the transplant was done. Therefore, regarding these two individuals no priority was given and no donor organs were wasted. Of the remaining ten patients who are presently all living, three are presently being supported on the artificial heart. Two of these are in Europe. The patient in the United States with the JARVIK-7 artificial heart represents the only case in which a donor organ has been lost. That patient, Bernadette Chayrez, had an ongoing viral disease at the time she received the JARVIK-7 artificial heart, was supported for four days, was transplanted on February 7, 1986 and rejected the transplanted heart two days later. She was then reimplanted with a second artificial heart and has been sustained since then by the device. Her condition has now improved sufficiently that Dr. Copeland tells me in the near future she may again become a transplant candidate. However, during this period of time she has not been on the transplant list because in her physicians judgment her condition did not warrant it. Of the remaining six patients who have received heart transplants, all are living, three are back at home and one has returned to work. Each of the patients who remain hospitalized has a reasonable hope of returning home. In all of these cases, the patients were not put on the active transplant list until their physicians ascertained that their condition was sufficient to expect success. In at least one case, a donor heart was available which was a suitable match for a patient sustained on the artificial heart. However, the team at that institution determined that another patient who was also awaiting transplant had a more urgent need for the heart and it was, therefore, given to that patient in preference to the patient on the JARVIK-7 heart.

I believe that experience with other total hearts is similar. At Hershey, Pennsylvania, Dr. Pierce has treated two bridge patients with a total artificial heart. Of these, one received a donor organ approximately three weeks after implant of the Penn State Heart and subsequently died of an infection approximately three weeks after the transplant. In a second case the patient was implanted with a Penn State Heart and at the present time has been sustained for approximately one and one half months with the device. I believe that the judgment of the Penn State team has been that the patient has not yet sufficiently recovered to be transplanted and that to date he has not been placed on the active transplant list. For more complete information, you may wish to consult Dr. Pierce.

Thus, in summary, our information shows that at eight different institutions where total artificial heart has been used as a bridge, patients have not been given preference to other patients awaiting heart transplantation solely because they were supported on artificial hearts but rather have been appropriately evaluated under the individual circumstance based on the greatest urgency of need for the available donor organs.

A second possible problem in a potential shift in priorities among transplant patients could be the use of donor organs in patients who were more severely ill than patients who would normally receive transplant. In such a circumstance it could be conceivable that these individuals might have many more complications than the present group of transplant candidates and the results could be worse resulting in some waste factor among the donor organs. There are two sides to this consideration. Two patients with active viral cardiomyopathy have been treated with the heart as a bridge and both cases have proven to be complicated, difficult and expensive. We have learned a great deal about viral cardiomyopathy and the immune system and are now certain that the nature of the disease process in these patients has made successful treatment very difficult. Indeed both patients are presently living and the knowledge gained most likely would permit treatment of additional patients with the condition with fewer complications and less expense. However, based on the knowledge we have gained so far we would recommend caution in this application. On the other hand, several of the physicians utilizing the artificial heart as a bridge-to-transplant have recognized that the period of time on the bridge device has permitted the physicial condition of the patients to be improved and that they are stronger at the time of the transplant surgery than many patients who have never had an artificial heart. It is possible that this factor could improve the results.

A third consideration of a shift in priorities, which I believe is a potential benefit, is the following. Presently our data indicates that heart attack patients can be saved by the bridge-to-transplant application. In the United States there are four hundred thousand deaths per year due to heart attacks and many of these are young individuals below the age of 45. In fact, only three of the twelve bridge patients have been older than 43. Heart attack victims usually are not able to become candidates for transplantation because they cannot wait. The availability of a successful artificial heart as a bridge device will bring some of these younger individuals into the candidate pool. Data shows that the long term survival of heart transplant patients in their thirties is better than that of patients in their forties which is in turn better than that of patients in their fifties. If priorities are shifted such that young heart attack patients wind up receiving a greater proportion of the available donor hearts and the long term survival statistics are indeed significantly better, the result could be an improvement in the number of patient survival years that can be obtained from each donor heart. Additionally, many of these younger people who now die suddenly of heart attacks are very productive members of society with an excellent prospect of rehabilitation.

Question: 2. You stated during the hearing that the artificial heart is used only in lifesaving situations. In view of this, do you believe FDA's draft emergency use policy should apply to the artificial heart or do you believe changes are necessary in the draft policy?

Response: I believe that the FDA's policy on emergency use of medical devices, should apply to the artificial heart. Symbion has clearly outlined our recommendations for changes in that policy and I am sure the committee has a copy of my letter which details our position. Since the hearing, I have met with FDA Commissioner Young and discussed this among other issues. It appears to me that the Commissioner is unlikely to adapt our recommendations and I find that disappointing. The FDA's policy is that an institution should not prepare for medical emergencies with unapproved devices. That policy is impractical. In fact, without appropriate preparation for use of a new medical device either approved or unapproved, its use, in my view, is ill advised. The FDA has taken the position that an unapproved device may only be used one time and, thereafter, may not be used again until it is approved. However, with the example of the small JARVIK-7 heart, after its first emergency use in Mary Lund, Dr. Copeland's team requested permission to use the device in Bernadette Chayrez and approval was granted. Thereafter, Dr. Bill Gay at the University of Utah requested emergency approval from the FDA to use the device in another patient. Approval was granted, however, at the last minute Dr. Gay was able to find that individual a transplant and the artificial heart was not needed. In a third specific instance, Dr. George Noon at Baylor requested permission from the FDA to use the small JARVIK-7 in a patient in desperate need of help and the FDA again granted permission. Shortly thereafter, that patient was judged to be too severely deteriorated to be helped with the device and the surgery was not done. However, this history has shown that the FDA, when faced with an individual patient in a life/death situation has felt that the small JARVIK-7 heart was appropriate to use despite the fact that this directly contradicts their emergency use policy. However, the Commissioner has personally expressed to me his view that the policy should be enforced even if it means denial is given to an identified patient who will then certainly die. I strongly disagree with the Commissioner's position and believe that, in fact, the FDA is following a policy which differs from their published guidelines. The policy of trusting the judgment of the individual physician when the team is trained and indeed prepared for the emergency, in my opinion, is correct.

The FDA is charged with protecting the public health and assessing the risk compared to the benefit. The following question is highly pertinent. Is the risk of the disease to be treated greater than the risk of the treatment to be used? If the answer is yes, especially where the risk of the disease is

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almost certain death and the benefit is a realistic possibility of life, then for the FDA to deny the use of the treatment through unncessarily stringent policies is detrimental to the public health.

Question: 3. Based on your experience with the permanent implants of the JARVIK-7 heart performed to date, how do you plan to modify the implant protocols for future implants approved by FDA?

- Will these changes in the implant protocols necessitate added review by the FDA?

Response: The protocol used at the Humana Heart Institute has been substantially modified following the FDA's panel review of permanent use on December 20, 1985. The modifications included many specific elements of patient management such as the requirement for more extensive testing of many additional factors related to the patient's coagulation system and to the patient's immune system. These changes have already been reviewed and approved by the FDA. However, the FDA has denied approval to permit use of the JARVIK-7 heart as a permanent device at the Minneapolis Heart Institute with Dr. Lyle Joyce as Principal Investigator and at St. Luke's Hospital in Phoenix with Dr. Cecile Vaughn as Principal Investigator. At the present time, Symbion does not plan to resubmit the two institutions requests which were denied. In the future, as more information is gained from the temporary use of the artificial heart together with the information on permanent use from Dr. DeVries' program and other programs abroad, we expect to again request approval for permanent use.

Question 4: I understand that all the data collected concerning the function of the artificial heart patients is considered by FDA to be confidential information. Given the high level of visibility which both these surgical procedures and the patients involved have received, what purpose is served by keeping this information from medical professionals - particularly when many surgeons have performed similar surgical transplants?

Response: There has been extensive collection of data and there are many efforts underway to publish a great deal of this information. Humana has several papers underway which we expect should be published soon. Dr. Jack Copeland together with the editors of the JOURNAL OF TRANSPLANTATION is working to publish many reports from the various centers which have performed artificial heart bridge operations in a single issue of the JOURNAL OF TRANSPLANTATION expected to be published late this summer or early fall.

The fact that strong interest from the medical profession has influenced the researchers in this field further supports the position that it is not the obligation of the FDA to participate in decisions concerning which scientific information should be published, when it should be published, or in what form. Protecting the confidentiality of the information submitted to the FDA protects the scientific investigators from premature release of their data and potentially erroneous conclusions which might be drawn from incomplete information. Furthermore, protecting the confidentiality of this information helps protect the rights of the appropriate medical researchers to receive recognition of their work through scientific publications in the journals of their choice.

Question 5: At present, Dr. DeVries is the only physician approved to implant the JARVIK-7 heart on a permanent basis. Is Symbion planning to apply for similar permission for any other investigators? If not, why?

Response: Presently, Symbion is not planning to apply for permission to implant the JARVIK-7 heart on a permanent basis at institutions other than the Humana Heart Institute. We believe that pressure on the FDA, particularly the visibility of the program, has made the FDA very sensitive about this issue. Symbion believes pursuing this, at the present time, would be harmful to its relationship with the FDA, although there are additional teams which wish permission to utilize the JARVIK-7 heart on a permanent basis. When we complete improvements of the artificial heart itself and have sufficient data to support the reasonable expectation of significantly improved results, we plan to ask the FDA for permission to expand to other institutions.

Question 6: It has been suggested that a multi-center review panel be formed to develop uniform standards related to the artificial heart implant protocol, patient selection criteria and minimum standards for the informed consent process, including forms. This panel would include, among others, representatives of the artificial heart manufacturers, the hospitals involved, and the appropriate physicians. Please comment.

Response: The artificial heart program has been subjected to an extensive amount of review. The effect of this review has been to slow the program and to significantly add to the cost of the research. In my opinion, little would be gained by an additional panel which would most likely further slow the program and probably not provide meaningful, additional protection for the patients. When the Medical Devices Act was passed by Congress, the issue of greater centralized regulation versus giving more weight to the opinion of the local Institutional Review Board was considered. As the law was enacted, the judgments of the local Institutional Review Boards were given considerable importance. Symbion believes that this was a reasonable decision and remains reasonable. However, if individuals such as Mr. Annis believe that the present law is inappropriate, it would be more reasonable if they addressed their efforts to changing the law rather than creating a special exception in the case of artificial hearts. I wish to remind the Committee that in every instance where the JARVIK-7 heart has been used in the United States, the medical teams have been trained and have had prior approval from their Institutional Review Boards. All cases have been conducted in accordance with the law. Furthermore, the results have been sufficiently good for many of this country's most prominent cardiac surgeons to participate directly in the research with the JARVIK-7 heart. We have had strong support from all the patients and their families and are confident that their rights have been protected to the best of our ability and that as we learn we can better deal with these issues. The present process is working and working well and, if anything, would be helped by less review rather than more.

I hope this information will be useful and if there is anything further I can do to be of assistance, please let me know.

Yours truly,

R. Jarvik MD

Robert K. Jarvik, M.D.
President
Symbion, Inc.

RKJ:rc

Statement of Symbion, Inc.

CHAIRMAN VOLKMER, COMMITTEE MEMBERS, GUESTS

THERE IS A COMMON REASON THAT WE ARE HERE TODAY. WE HAVE IN THIS COUNTRY A BELIEF IN SCIENCE AND TECHNOLOGY, AS A FOUNDATION OF OUR HERITAGE AND AS A CORNERSTONE OF OUR FUTURE. AND WE HAVE A DEDICATION TO PRESERVE AND EXPAND OUR FREEDOM AND TO APPLY OUR RECOGNITION OF THE VALUE OF EACH HUMAN LIFE TO IMPROVE OUR SOCIETY. THE CHALLENGE IS TO BRING WARMTH TO SCIENCE AND TO APPLY TECHNOLOGY IN LINE WITH OUR HUMAN VALUES. THE CHALLENGE IS TO COMBINE THEM. TO BRING THEM TOGETHER.

NOWHERE IS THIS MORE APPARENT THAN WITH THE ARTIFICIAL HEART. AND AT NO TIME IN OUR HISTORY, HAS IS BEEN MORE APPARENT THAT AMERICANS CARE ABOUT THE HUMAN SIDE OF OUR SCIENTIFIC EFFORTS. AT NASA'S REQUEST I SERVED AS A JUDGE IN THE SELECTION OF THE TEN FINALISTS FOR THE TEACHER IN SPACE PROGRAM. I MET CHRISTA MCAULIFFE AT THE WHITE HOUSE. I RANKED HER 10 1/2 ON MY FINAL SELECTION SCALE - ABOVE ANY OTHER CANDIDATE. I VOTED FOR HER AND I WAS DELIGHTED WHEN SHE WAS CHOSEN. AND LAST WEEK WHEN SHE DIED - MY THOUGHTS TURNED TO MARY LUND, ANOTHER YOUNG WOMAN ON THE VERY BRINK OF IT ALL - LIVING WITH THE JARVIK-7® HEART, HOPING THAT THEY WILL FIND HER A TRANSPLANT.

CHRISTA'S DEATH WAS ONE OF A SERIES OF EVENTS THAT I HAVE FELT VERY PERSONALLY. FROM THE SELFLESS WILLINGNESS TO ENTER THE UNKNOWN THAT MEN SUCH AS BARNEY CLARK AND BILL SCHROEDER HAVE SHOWN, TO THE ELATION THAT OTHERS WITH THE ARTIFICIAL HEART HAVE FELT. THOSE WHO HAVE TRUELY DONE WELL. LEIF STENBERG, MICHAEL DRUMMOND, THOMAS GAIDOSH.

MICHAEL RECENTLY WROTE THESE SIMPLE WORDS TO ME "BEST OF LUCK IN YOUR FUTURE WITH THE DEVICE THAT SAVED MY LIVE." THAT SAYS IT ALL.

WE ARE HERE TODAY BECAUSE THE ARTIFICIAL HEART CAN MAKE A DIFFERENCE. AND BECAUSE THERE ARE FEW FRONTIERS AS CLEAR AS SPACE. THIS IS ONE OF THEM. BUT MOSTLY BECAUSE THERE IS AN OVERWHELMING MEDICAL NEED. HEART DISEASE KILLS A MILLION AMERICANS EACH YEAR; AS MANY AS ALL OTHER DISEASES COMBINED. HEART ATTACKS WILL KILL 500 PEOPLE TODAY - WHILE WE HOLD THESE HEARINGS. ANOTHER 500 BY TOMORROW MORNING. AND ON AND ON. THE PUBLIC CARES INTENSELY ABOUT MEDICAL PROGRESS IN THIS FIELD. ARTIFICIAL HEART HAS OUR ATTENTION. IT HAS BECOME A SYMBOLIC FOCUS OF MANY EFFORTS TO APPROACH THE PROBLEM THROUGH MEDICAL SCIENCE AND TECHNOLOGY. BUT ALSO IT MAY PROVIDE A MODEL OF COOPERATION AND POSITIVISM THAT AMERICA CAN WELL USE.

WE DO NOT PRETEND THAT THE ARTIFICIAL HEART IS THE SOLE ANSWER. BUT IT IS BECOMING PART OF THE ANSWER. HEART DISEASE WILL ONLY BE MARKEDLY REDUCED THROUGH A COMBINATION OF EFFORTS - INCLUDING ADVANCES IN DRUGS, NEW METHODS SUCH AS CORONARY ANGIOPLASTY AND ABOVE ALL - PREVENTIVE MEDICINE. THERE IS NO DOUBT OF THE DEVISTATING EFFECTS OF SMOKING, OBESITY, AND HYPERTENSION. I SPEAK IN FAVOR OF PREVENTION AT EVERY OPPORTUNITY. I SUPPORT LEGISLATION TO ELIMINATE

ALL CIGARETTE ADVERTISING. I DON'T SMOKE, I EXERCISE REGULARLY AND I AM ONLY 7% BODY FAT - SOMETHING LESS THAN OBESE. I CAN'T SAY I LIVE A LIFE ENTIRELY FREE OF STRESS. EDITORIALS SUCH AS A RECENT ONE IN THE NEW YORK TIMES ENTITLED "THE HEART THAT FIZZLED" SOMETIMES SEND MY BLOOD PRESURE THROUGH THE ROOF. BUT AFTER 15 YEARS OF WORK ON THIS PROGRAM, I HAVE BECOME CONVINDED THAT ARTIFICIAL HEARTS WILL BE PRACTICAL, WILL PROVIDE A HIGH QUALITY OF LIFE FOR TENS OF THOUSANDS OF AMERICANS, AND WILL BE COST EFFECTIVE.

WE FACE MANY CHALLENGES, BUT I AM SURE WE WILL SUCCEED FOR THESE REASONS: ARTIFICIAL HEART TECHNOLOGY IS FUNDAMENTALLY SOUND; IT WORKS; IT HAS BEEN DEVELOPED THROUGHT DECADES OF INTENSIVE RESEARCH...THE HEART LUNG MACHINE, THE INTRA-AORTIC BALLOON PUMP, THE LEFT HEART ASSIST DEVICE, THE TOTAL ARTIFICIAL HEART. THESE ALL SHARE COMMON ELEMENTS OF BLOOD PUMPING TECHNOLOGY SUCCESSFULLY APPLIED IN HUNDREDS OF THOUSANDS OF PATIENTS EACH YEAR. TECHNOLOGY IN BIOMATERIALS, VASCULAR GRAFTS AND PROSTETIC HEART VALVES IS ADVANCED. TECHNIQUES IN CARDIAC SURGERY AND POSTOPERATIVE CARE ARE WELL DEVELOPED. AND PERHAPS MOST IMPORTANTLY - MANY HUNDREDS OF TALENTED AND DEDICATED SPECIALISTS IN MEDICINE, ENGINEERING AND NUMEROUS RELEVANT DISCIPLINES ARE WILLING TO CONTINUE WORKING TOGETHER TO MAKE THE ARTIFICIAL HEART PROGRAM SUCCEED. THE AMERICAN PUBLIC WANTS SUCCESS THE GOAL IS UNDISPUTED - A HIGH QUALITY LIFE - AVAILABLE TO ALL OUR CITIZENS - AT A REASONABLE COST. WE KNOW WHAT WE ARE WORKING TO ACCOMPLISH.

I HAVE FREQUENTLY BEEN REFERRED TO AS THE INVENTOR OF THE ARTIFICIAL HEART. I AM NOT, ALTHOUGH I HAVE INVENTED SOME CRUCIAL ELEMENTS OF THE SYSTEM. THE BASIC FUNCITONAL CONCEPT DATES BACK TO THE WORK OF KOLFF, AKUTSU, DEBAKEY, LIOTTA, KWAN-GETT AND OTHERS WHO CONTRIBUTED TO THE EVOLUTION OF THIS TYPE OF BLOOD PUMP IN THE LATE 50S AND THE DECADE OF THE 60S. WE HAVE LEARNED THAT A VERY SIMPLE PUMPING MECHANISM CAN EFFECTIVELY REPLACE THE NATURAL HEART AND THAT HUMAN PATIENTS CAN BE SUSTAINED WITH EXCELLENT HEMODYNAMIC FUNCTION FOR MORE THAN A YEAR. PERHAPS MY MAJOR TECHNICAL CONTRIBUTION HAS BEEN THE DEVELOPMENT OF THE MULTILAYERED-GRAPHITE LUBRICATED POLYURETHANE DIAPHRAGM WHICH MUST FLUX 40 MILLION CYCLES PER YEAR FORTY MILLION HEART BEATS AND ROUTINELY LASTS 4-5 YEARS IN JARVIK-7 HEARTS TESTED ON THE MOCK CIRCULATION. PREVIOUS POLYURETHANE DIAPHRAMS BROKE WITHIN ONE MONTH. I BELIEVE WE WILL FURTHER IMPROVE THE DESIGN AND THAT HIGHLY RELIABLE HEARTS WILL PUMP EIGHT TO TEN YEARS WITHOUT FAILURE.

ANIMAL RESEARCH WITH THE JARVIK-7 HEART AND ITS PREDECESSORS WAS FUNDED BY THE NATIONAL INSTITUTE OF HEALTH FOR MANY YEARS. WITH THIS SUPPORT DR. DON OLSEN AND HIS TEAM, AT THE UNIVERSITY OF UTAH, MADE MAJOR CONTRIBUTIONS IN SURGICAL TECHNIQUE, POSTOPERATIVE CARE, AND PHYSIOLOGICAL EVALUATION. NIH IS ALSO SUPPORTING MANY OTHER RELATED PROGRAMS AND THERE IS EXTENSIVE SCIENTIFIC LITERATURE IN THE FIELD. I BELIEVE THAT THE LEVEL OF NIH FUNDING PRESENTLY PLANNED FOR THE ARTIFICIAL HEART OVER THE NEXT SEVERAL YEARS REPRESENTS INADEQUATE FOLLOWTHROUGH ON THE 200 MILLION DOLLAR GOVERNMENT

INVESTMENT IN THIS TECHNOLOGY TO DATE. A GREATLY EXPANDED PROGRAM INCLUDING CLINICAL EVALUATIONS OF PNEUMATIC SYSTEMS AS A STEP TOWARDS DEVELOPMENT OF MORE DESIRABLE ELECTRIC SYSTEMS, WOULD HELP THE UNITED STATES RETAIN THE LEADERSHIP IT NOW HOLDS.

THE DECISION TO BEGIN HUMAN STUDIES WITH THE JARVIK-7 HEART WAS BASED ON OUR SUBSTANTIATED BELIEF THAT WE COULD OFFER REAL HOPE OF AN EXTENDED AND IMPROVED LIFE TO PATIENTS WHO OTHERWISE FACED CERTAIN DEATH - AND THAT WE COULD GAIN IMPORTANT SCIENTIFIC KNOWLEDGE.

BARNEY CLARK SAW THE ANIMALS WITH ARTIFICIAL HEARTS SIX WEEKS BEFORE HIS SURGERY. HE UNDERSTOOD WHAT TO EXPECT AND HAD TIME TO THINK ABOUT IT. HIS CONSENT WAS THOROUGHLY INFORMED. THE PROTOCOL FOR THIS FIRST CASE TOOK MORE THAN 2 YEARS TO DEVELOP AND APPROVE. ETHICAL CONSIDERATIONS WERE PARAMOUNT.

BEAR IN MIND THAT THE BASIC INDICATION FOR USE OF THE ARTIFICIAL HEART AND REMAINS UNCHANGED TODAY. THE PATIENT MUST FACE IMMINENT DEATH, WHEN NO OTHER MEDICAL TREATMENT IS JUDGED TO HAVE A REASONABLE CHANCE OF SUCCESS, AND INFORMED CONSENT IS GRANTED BY THE PATIENT OR A RESPONSIBLE FAMILY MEMBER.

THE ARTIFICIAL HEART IS NOT IMPLANTED IN ANY PATIENT WHO IS A TRANSPLANT CANDIDATE AND CAN WAIT ANY LONGER FOR A DONOR ORGAN. ONLY WHEN WAITING FOR A DONOR IS NO LONGER POSSIBLE, CAN THE ARTIFICIAL HEART BE USED.

TO DATE, THREE SUCH CASES HAVE BEEN DONE WITH THE JARVIK-7 HEART. TWO OF THE PATIENTS ARE AT HOME AND IN EXCELLENT CONDITION AFTER THE ARTIFICIAL HEART WAS REMOVED AND THE TRANSPLANT PERFORMED. MARY LUND, IS STILL AWAITING A DONOR HEART AND HAS VERY REAL HOPE.

WE HAVE HAD FIVE CASES OF PERMANENT USE. BILL SCHROEDER IS ALIVE 14 MONTHS AFTER THE IMPLANT. HE HAS BEEN IN FAR BETTER CONDITION THAN BARNEY CLARK. HE HAS LIVED IN AN APARTMENT NEAR THE HOSPITAL AND HAS REVISITED HIS HOME IN JASPER, INDIANA. BUT HE HAS BEEN SEVERELY HANDICAPPED BY THE EFFECTS OF HIS STROKES AND MY RESPECT FOR HIS COURAGE AND FORTITUDE IS EVER INCREASING. HIS FAMILY AS WELL AS DR. DEVRIES AND THE HUMANA TEAM HAVE RETAINED THEIR DEEP COMMITTMENT TO HIM THROUGH SUCH DIFFICULT TIMES. IT IS A STORY OF BOTH TRIUMPH AND TRAGEDY. MURRAY HAYDEN HAS BEEN LIVING ALMOST ONE YEAR WITH HIS IMPLANT. FIVE MONTHS AFTER SURGERY HE SUFFERED A MINOR STROKE FROM WHICH HE RECOVERED COMPLETELY IN A FEW DAYS. HE IS NOW NEUROLOGICALLY NORMAL WITH NO EVIDENCE OF THROMBOEMBOLISM. HE HAS HAD CONTINUING PROBLEMS WITH LUNG FUNCTION DUE TO A POST SURGICAL BLEEDING PROBLEM WHEN A MONITORING CATHETER WAS REMOVED. THIS HAS NOTHING TO DO WITH THE HEART ITSELF. LEIF STENBERG SURVIVED 7 1/2 MONTHS. HE WAS IN DISMAL CONDITION AT THE TIME OF THE IMPLANT. HE

REGAINED STRENGTH AND FREQUENTLY LEFT THE HOSPITAL WITH THE PORTABLE DRIVE SYSTEM. HE VISITED FRIENDS, WENT OUT TO RESTAURANTS AND EVEN WALKED UP FIVE FLIGHTS OF STAIRS TO ATTEND A BIRTHDAY PARTY AT HIS SON'S APPARTMENT. HE ULTIMATELY DIED FOLLOWING A SEVERE BRAIN HEMORRHAGE, RELATED TO INFECTION AND THROMBOEMBOLISM. JACK BURCHAM DIED 10 DAYS AFTER SURGERY FROM BLEEDING, RELATED IN PART TO POOR FIT OF THE HEART IN HIS CHEST. HE HAD A DEFORMITY OF HIS RIB CAGE WHICH MADE FIT DIFFICULT AND WE DID NOT HAVE A SMALL SIZE HEART AVAILABLE AS A BACKUP.

THUS, OF THE EIGHT PATIENTS - FIVE ARE ALIVE TODAY. THE AVERAGE SURVIVAL OF THE PERMANENT USE PATIENTS IS ABOUT 7 1/2 MONTHS. THEIR LIFE EXPECTANCY WITHOUT IT WAS A MATTER OF HOURS OR DAYS. WE HAVE DEMONSTRATED THAT A HIGH QUALITY OF LIFE IS POSSIBLE.

WE HAVE LEARNED A GREAT DEAL ABOUT THE MEDICAL MANAGEMENT OF THESE PATIENTS. WE HAVE HAD FEW EQUIPMENT PROBLEMS AND NO CATASTROPHIC DEVICE FAILURES. WE WELL UNDERSTAND THE AREAS IN THE HEART ITSELF THAT ARE SUSCEPTIBLE TO THROMBUS FORMATION IF ANTICOAGULATION IS NOT ADEQUATE. WE HAVE TESTED DESIGNS IN ANIMALS WHICH ARE A SIGNIFICANT IMPROVEMENT AND ARE IN THE PROCESS OF FINALIZING A DESIGN MODIFICATION WHICH I STRONGLY BELIEVE WILL VERY GREATLY REDUCE THE RISK OF STROKE. SO FAR, WE HAVE EVIDENCE THAT THE ARTIFICIAL HEART IS FREE OF CALCIFICATION IN HUMANS. THIS HAS BEEN A SEVERE PROBLEM IN CALVES.

I BELIEVE FUTURE WORK, BOTH WITH BRIDGE TO TRANSPLANT AND PERMANENT USE IS APPROPRIATE. THERE ARE A WIDE RANGE OF SCIENTIFIC QUESTIONS OF INTEREST WHICH CANNOT BE ANSWERED WITHOUT MANY MANY MORE HUMAN CASES. SYMBION HAS TRAINED NINE TEAMS IN THE UNITED STATES AND FOUR ABROAD TO IMPLANT THE HEART. THE PRINCIPAL INVESTIGATORS INCLUDE - DR. DEVRIES, DR. COPELAND, DR. JOYCE, DR. GRIFFITH AND DR. SEMB - ALL OF WHOM SUCCESSFULLY IMPLANTED THE HEART IN THEIR PATIENTS. OTHERS WHO WILL SOON BEGIN INCLUDE DR. FRAZIER AND DR. COOLEY, DR. NOON AND DR. DEBAKEY, DR. GAY, DR. TECTOR AND DR. VAUGHN. ABROAD SOME LEADING TRANSPLANT EXPERTS INCLUDING DR. ENGLISH IN CAMBRIDGE, ENGLAND, DR. CABROL IN PARIS, FRANCE, AND DR. KEON IN OTTAWA, CANADA HAVE COMPLETED THEIR TRAINING. THE EXTENSIVE KNOWLEDGE OF THESE PHYSICIANS AND THE COMMITTMENT OF THEIR INSTITUTIONS SPEAKS HIGHLY OF THE CONFIDENCE THE MEDICAL COMMUNITY HAS THAT HUMAN APPLICATION OF THE JARVIK-7 HEART IS WORTHWHILE.

IT IS REVEALING TO CONSIDER THE HISTORY OF OTHER NEW INNOVATIONS IN MEDICINE. HEART TRANSPLANT NOW ACHIEVES 70-80% ONE YEAR SURVIVAL WITH AN EXCELLENT QUALITY OF LIFE. IT WAS NOT ALWAYS SO. OF THE FIRST FIFTY PATIENTS TO UNDERGO HUMAN HEART TRANSPLANT EIGHT DIED FROM THROMBOEMBOLISM OR STROKE. THATS 16%. WITH THE FIRST EIGHT JARVIK-7 HEART PATIENTS, ONE DIED FROM COMPLICATIONS RELATED TO THROMBOEMBOLISM OR STROKE. THATS 12.5%. OF THE TRANSPLANT PATIENTS, NINE DIED OF HEART FAILURE AND FOUR FROM INFECTION. OF THE ARTIFICIAL HEART PATIENTS, NONE HAVE DIED OF HEART FAILURE, TWO HAVE DIED FROM INFECTION. THESE ARE THE SAME PROBLEMS

THAT WE ARE WORKING TO OVERCOME WITH THE ARTIFICIAL HEART BUT THE PUBLIC DOESN'T REALIZE THAT THEY ARE LESS SEVERE THAN WITH THE INITIAL USE OF TRANSPLANT. OF THE FIRST FIFTY TRANPLANT PATIENTS, TWENTY ONE DIED IN LESS THAN A WEEK. THATS 42%. NONE OF OUR ARTIFICIAL HEART PATIENTS HAVE DIED IN LESS HAN ONE WEEK. WITH THE INITIAL TRANSPLANT GROUP, ELEVEN SURVIVED MORE THAN SIX MONTHS. THATS 22% WITH THE PERMANENT TOTAL HEART - THREE OF FIVE HAVE SURVIVED MORE THAN SIX MONTHS. THATS 60% - ABOUT THREE TIMES AS MANY LONG TERM SURVIVORS AS WITH TRANSPLANT.

HAD THE INITIAL RESULTS WITH TRANSPLANT BEEN AS GOOD AS OUR INITIAL ARTIFICIAL HEART RESULTS, TRANSPLANT MAY HAVE BECOME MORE WIDELY APPLIED FASTER. IT IS ALSO IMPORTANT TO NOTE THAT ALTHOUGH THE FDA WAS NOT INVOLVED, TRANSPLANT DID NOT BECOME WIDESPREAD UNTIL THE MEDICAL COMMUNITY AND THE PUBLIC FELT THE RESULTS WARRANTED IT.

THE FIRST FIFTEEN PATIENTS TREATED WITH ARTIFICIAL KIDNEYS DIED WITHIN DAYS, BUT NOW 250,000 PEOPLE ARE SUSTAINED WITH DIALYSIS FOR MANY YEARS OF WORTHWHILE LIFE.

THE FIRST CARDIAC PACEMAKERS WERE THE SIZE OF A TELEVISION SET AND WERE WHEELED AROUND WITH THE PATIENT ON A CART. THEY ARE NOW ABOUT THE SIZE OF A STACK OF THREE OR FOUR SILVER DOLLARS. THEY LAST RELIABLY FOR MORE THAN TEN YEARS.

THERE ARE COUNTLESS OTHER EXAMPLES.

WE FACE SERIOUS PROBLEMS REGARDING FEDERAL REVIEW AND REGULATION OF THE ARTIFICIAL HEART. SYMBION HAS MADE EVERY EFFORT TO COOPERATE EFFECIVELY WITH THE FDA. SINCE 1980 WE HAVE MAINTAINED AN EXTENSIVE CORRESPONDENCE WITH THE FDA WHICH NOW INCLUDES OVER 2,600 PAGES OF DOCUMENTS. FDA OFFICIALS HAVE VISITED SYMBION AND HAVE PARTICIPATED WITH US IN SEVERAL FORUMS DEALING WITH THE ISSUES, INCLUDING A MAJOR CONFERENCE SYMBION SPONSORED ON THE ARTIFICIAL HEART AND PUBLIC POLICY. WE HAVE FREQUENTLY VISITED FDA OFFICIALS IN WASHINGTON. COMMISSIONER YOUNG HAS TAKEN AN ACTIVE PERSONAL INTEREST IN THE PROGRAM - ESPECIALLY THE EMERGENCY USE GUIDELINES.

ARTIFICIAL HEART NEED NOT REQUIRE SO MUCH ATTENTION FROM THE FDA. DR. DWIGHT HARKEN, CLINICAL PROFESSOR OF SURGERY (EMERITUS), OF HARVARD MEDICAL SCHOOL HAS SAID "A DEVICE IS SAFE WHEN IT IS SAFER THAN THE DISEASE IT TREATS AND IT IS THE BEST AVAILABLE." I BELIEVE THAT IN APPROPRIATE PATIENTS THE ARTIFICIAL HEART IS FAR SAFER THAN ANY OTHER AVAILABLE TREATMENT.

I BELIEVE THE FDA IS HAVING DIFFICULTY BECAUSE THE LAW REQUIRES THEM TO ASSESS RISK BENEFIT RATIO AND JUDGE QUALITY OF LIFE. IN MY VIEW, A RISK IS ACCEPTABLE WHEN THE PERSON AT RISK UNDERSTANDS IT AND ACCEPTS IT. VERY SIMPLE.

REGARDING QUALITY OF LIFE, I BELIEVE THE FDA HAS NO CHOICE BUT TO DECIDE THAT LIFE IS ALWAYS PREFERABLE TO DEATH. I PERSONALLY BELIEVE THAT THERE ARE MANY THINGS WORSE THAN DEATH AND THAT PROLONGING SUFFERING IS ONE OF THEM. THAT IS NOT WHAT THE ARTIFICIAL HEART DOES AND IF IT WERE, I WOULD NOT CONTINUE TO WORK WITH IT. BUT THE SUBJECTIVE DECISION - OF WHEN THE RISK OF A POSSIBLE COMPLICATION IS SO HIGH THAT A PATIENT SHOULD NOT BE ALLOWED THE CHOICE - AND THE LAW SHOULD THEREBY MANDATE HIS OR HER DEATH - THAT DECISION SHOULD NOT BE A MATTER OF LAW. IT SHOULD REMAIN BETWEEN THE PATIENT AND THE PHYSICIAN. I BELIEVE THAT THE MEDICAL DEVICES ACT OF 1976 IS RIGHT TO REQUIRE INFORMED CONSENT TO THE FULLEST EXTENT PRACTICAL. PATIENTS CANNOT UNDERSTAND EVERYTHING AND AN ESSENTIAL ELEMENT MUST BE TRUST IN THE PHYSICIANS JUDGMENT. THE LAW MUST NOT INTERFERE WITH THE BASIC DOCTOR-PATIENT RELATIONSHIP OF TRUST AND COMMITTMENT - LONG ACCEPTED AS THE BASIS OF MEDICAL ETHICS AND SO WELL EXPRESSED TWO THOUSAND YEARS AGO IN THE OATH OF HIPPOCRATES.

THE 1976 MEDICAL DEVICES ACT PROVIDED A MECHANISM CALLED THE INVESTIGATIONAL DEVICE EXEMPTION WHICH WAS INTENDED TO FACILITATE THE INTRUDUCTION OF IMPORTANT NEW ADVANCES. A LARGE PORTION OF THE RESPONSIBILITY FOR REVIEW WAS PLACED ON THE LOCAL INSTITUTIONAL REVIEW BOARDS. I BELIEVE CONGRESS WAS WISE IN THAT DECISION AND IT SHOULD NOT BE CHANGED.

SYMBION HAS TAKEN A CLEAR POSITION REGARDING EMERGENCY USE OF LIFESAVING MEDICAL DEVICES. THAT IS, THAT AFTER THE INSTITUTIONAL REVIEW BOARD HAS APPROVED USE, THE DEVICE SHOULD BE PERMITTED TO BE AVAILABLE FOR USE IN AN EMERGENCY - EVEN THOUGH THE FDA MAY NOT HAVE HAD TIME TO COMPLETE ITS REVIEW. PHYSICIANS AND TEAMS WHICH HAVE MADE THE EFFORT TO PREPARE AND OBTAIN IRB APPROVAL ARE PLACED IN AN UNTENABLE POSITION IF THEY MUST DENY THE USE OF A NEW TECHNOLOGY THEY BELIEVE IN TO THEIR OWN PATIENTS - WHO MAY BE DYING BEFORE THEIR VERY EYES. FIGURATIVELY, WE CANNOT INVENT LIFE JACKETS AND THEN PROHIBIT THEIR USE UNTIL WE EVALUATE THE STRAPS AND BUCKLES OR DECIDE WHETHER THEY SHOULD BE YELLOW OR ORANGE. THE LAW SHOULD RECOGNIZE RESPONSIBILITY FOR DENIAL OF LIFE SAVING TECHNOLOGY AS WELL AS THE NEED TO INSURE THAT WE MAXIMIZE THE SAFETY OF MEDICAL DEVICES. WE NEED TO WISELY BALANCE THESE TWO RESPONSIBILITIES.

I HOPE CONGRESS WILL HELP RELIEVE SOME OF THE PRESSURE FDA IS UNDER BECAUSE OF THE EXTENSIVE PUBLICITY OF THE ARTIFICIAL HEART. USUALLY AN INVESTIGATIONAL DEVICE EXEMPTION PERMITS TESTING IN SEVERAL HUNDRED OR EVEN A THOUSAND PATIENTS PRIOR TO PRE-MARKET APPROVAL. I BELIEVE IT IS PROVEN WITHOUT A DOUBT THAT THE JARVIK-7 HEART DOES SAVE LIVES AND THAT THERE IS NOW ENOUGH DATA FOR THE FDA TO TREAT IT IN THE SAME WAY OTHER NEW DEVICES ARE HANDLED.

I BELIEVE IT IS APPROPRIATE TO APPROVE ADDITIONAL INSTITUTIONS TO STUDY THE ARTIFICIAL HEART. I BELIEVE THE REVIEW OF RESULTS WITH THESE STUDIES NEED NOT BE MORE STRENUOUS THAN WITH OTHER

NEW LIFE SAVING MEDICAL DEVICES. YET, TO DATE, I BELIEVE IT HAS BEEN. THE INCREASED REPORTING REQUIREMENTS THAT DR. DEVRIES FACES - FOLLOWING REVIEW OF HIS PROGRAM BY THE FDA ADVISORY PANEL AND THE RESTRICTION TO NO MORE THAN ONE PATIENT EVERY THREE MONTHS - IN MY VIEW - MANDATES DELAY. DR. DAVID SKINNER, CHAIRMAN OF SURGERY AT THE UNIVERSITY OF CHICAGO HAS SAID, "THE ONLY QUESTION REMAINING ABOUT ARTIFICIAL HEART IS WHETHER IT WILL BE AN IMPORT OR AN EXPORT." THE DENIAL OF APPROVAL TO USE THE JARVIK-7 HEART AS A PERMANENT DEVICE AT OTHER INSTITUTIONS UNTIL DR. DEVRIES COMPLETES HIS SERIES OF SEVEN CASES IS FORCING US TO TAKE THE PROGRAM ABROAD. WE HAVE MANY EXCELLENT MEDICAL SCIENTISTS IN THIS COUNTRY WHO HAVE THE COMMITTMENT AND THE RESOURCES TO BE WORLD LEADERS, IF OUR GOVERNMENT WOULD TRUST THEM AND ENCOURAGE THEM.

FINALLY, I WOULD LIKE TO BREIFLY ADDRESS AN ISSUE OF ECONOMICS. I AM PRESIDENT OF SYMBION, INC., A SMALL PUBLICLY HELD COMPANY, AND I ACUTELY RECOGNIZE THAT NEW TECHNOLOGIES SPAWNED BY GOVERNMENT FINANCED UNIVERSITY RESEARCH CAN ONLY BECOME OF WIDESPREAD BENEFIT TO THE PUBLIC IF THEY CAN BE PRODUCED PROFITABLY. I BELIEVE IN FREE ENTERPRISE. I BELIEVE OUR FUTURE BENEFITS FROM ENTREPRENEUREAL SUCCESS. I RECOGNIZE IN THE ARTIFICIAL HEART TWO THINGS. ONE THAT IT WILL ONLY BE BROADLY APPLIED WHEN IT'S SUCCESS AND VALUE IS INHERENTLY OBVIOUS TO THE PUBLIC. UNTIL IT WORKS VERY WELL INDEED, IT WILL CONSUME AN INSIGNIFICANT PORTION OF OUR NATIONAL RESOURCES. AND TWO, UNLESS OUR SYSTEM, SUPPORTED BY GOVERNMENT, NOT IMPEDED, CAN MOVE QUICKLY ENOUGH, THEN FREE ENTERPRISE - ESPECIALLY

THROUGH SMALL BUSINESS - CANNOT SUCCEED WITH MAJOR ADVANCES SUCH AS THIS. SYMBION HAS INVESTED HEAVILY IN RESEARCH AND DEVELOPMENT. OUR LOSSES ATTRIBUTABLE TO THE ARTIFICIAL HEART SIDE OF OUR BUSINESS EXCEED $500,000 FOR EACH HUMAN CASE DONE SO FAR.

I WOULD HOPE THAT CONGRESS COULD HELP US. BY AFFIRMING THAT IT IS IN THE PUBLIC INTEREST TO ACHIEVE AN EXCELLENT - VALUE EFFECTIVE ARTIFICIAL HEART - SOONER RATHER THAN LATER. BY AFFIRMING THAT WORLD LEADERSHIP IN SCIENCE IS AN AMERICAN GOAL - AND ARTIFICIAL HEART IS PART OF IT. BY RECOGNIZING THE EDUCATIONAL IMPACT OF OUR WORK AND THE INTEREST WE ARE GENERATING AMONG THE NATION'S YOUTH - AND BY AFFIRMING AGAIN, THAT THE APPLICATION OF SCIENCE AND TECHNOLOGY TO THE BENEFIT OF HUMANITY IS INDEED ONE THING AMERICA DOES WELL.

THANK YOU.

Remarks to the F.D.A. advisory panel by R.K. Jarvik, M.D., President of Symbion, Inc.

12/19/85

GOOD MORNING. AS SPONSOR OF THE HUMAN CLINICAL INVESTIGATIONS WITH THE JARVIK 7 HEART SYMBION APPRECIATES THIS OPPORTUNITY TO PARTICIPATE IN TODAY'S REVIEW OF THE INITIAL RESULTS OF OUR ONGOING RESEARCH. I APPRECIATE THE EFFORTS OF EACH MEMBER OF THE PANEL AND UNDERSTAND THE TIME AND EFFORT YOU HAVE COMMITTED TO ASSISTING THIS PROCESS. SYMBION WAS FORMED IN 1976. I HAVE PERSONALLY BEEN INVOLVED IN ARTIFICIAL HEART RESEARCH FOR OVER 15 YEARS. AS I LOOK AROUND THIS ROOM, I SEE MANY INDIVIDUALS OF BROADLY DIVERSE BACKGROUNDS AND EXPERTISE, WHO HAVE WORKED TIRELESSLY TOWARDS THE ALLEVIATION OF SUFFERING FROM HEART DISEASE. ALTHOUGH WE ARE HERE TODAY TO REVIEW THE PROGRESS WITH THE PERMANENT TOTAL ARTIFICIAL HEART, WE SHOULD NOT OVERLOOK THE FACT THAT A GREAT DEAL OF EXCELLENT SCIENTIFIC RESEARCH HAS BEEN CONDUCTED WITH OTHER MECHANICAL CIRCULATORY SUPPORT DEVICES, IN HUNDREDS OF HUMAN PATIENTS. ARTIFICIAL HEART RESEARCH IS A VERY BROADLY INTERDISCIPLINARY ENDEAVOR-INVOLVING MANY FRONTIERS IN MEDICINE, ENGINEERING, ETHICS AND ALSO PUBLIC POLICY. IT CANNOT BE VIEWED AS PURE SCIENCE, IN A VACUUM, OR AS A SOLELY HUMANATIAN EFFORT, OR AS FOREMOST AN IDEALIZED ETHICAL DILEMMA OR AS A SYMBOLIC FOCUS FOR EDUCATIONAL OR OTHER OBJECTIVES. THIS WORK, IN WHICH ALL OF US ARE TOGETHER INVOLVED, IS FUNDAMENTALLY A COOPERATIVE VENTURE WITH SOME VERY CLEAR OBJECTIVES. SYMBION HAS WORKED TOGETHER WITH HUNDREDS OF INDIVIDUALS AND MANY MAJOR INSTITUTIONS. I AM CONTINUALLY IMPRESSED WITH THE ENERGY, PASSION, AND DEDICATION PEOPLE PUT

INTO THIS THING. WE ARE WORKING HARD TO COOPERATE EFFECTIVELY WITH THE FDA AND TO REMAIN IN COMPLIANCE WITH THE MEDICAL DEVICE REGULATIONS. SYMBION AND THE FDA SHARE MANY COMMON GOALS AND INTERESTS. WE BOTH ARE COMMITTED TO ASSURE THAT ARTIFICIAL HEARTS WILL BE SAFE AND EFFECTIVE AND WE BOTH SEEK TO MINIMIZE THE RISKS AND MAXIMIZE THE BENEFITS.

LET ME SHARE SOME OF SYMBION'S ADDITIONAL PERSPECTIVES WITH YOU. WE ARE TALKING ABOUT A TECHNOLOGICAL APPROACH TO HEART DISEASE - ONE OF MANY APPROACHES TO A HEALTH PROBLEM OF STAGGERING MAGNITUDE. CARDIOVASCULAR REMAINS THE NUMBER ONE KILLER IN THE UNITED STATES.

IN 1984 IT TOOK MORE THAN A MILLION LIVES - NEARLY DOUBLE THE NUMBER OF DEATHS DUE TO CANCER AND ROUGHLY EQUAL TO ALL OTHER CAUSES OF DEATH COMBINED. AMERICAN HEART ASSOCIATION FIGURES FOR 1984 PLACE THE TOTAL COST AT $64.4 BILLION INCLUDING THE ESTIMATED OF LOST OUTPUT OF $12.4 BILLION DUE TO DISABILITY. THIS - DESPITE THE FACT THAT IN THE PAST DECADE THE DEATH RATE FROM CARDIOVASCULAR DISEASE HAS DROPPED BY MORE THAN 20%. ADVANCES IN PHARMACOLOGY, EMERGENCY CARDIAC CARE, CARDIAC SURGERY, AND NEW TREATMENT METHODS SUCH AS ANGIOPLASTY ARE IMPORTANT AND ARE CONTRIBUTING TO THIS DECLINE. INCREASED ATTENTION TO PREVENTIVE MEASURES, INCLUDING CHANGES IN DIET, INCREASED EXERCISE AND DECREASED SMOKING ALSO HAVE PLAYED A SIGNIFICANT ROLE. SYMBION STRONGLY SUPPORTS ALL OF THESE EFFORTS.

IT IS IMPORTANT TO KEEP THESE FACTS IN MIND. IT ALSO IS IMPORTANT TO RECOGNIZE THAT THE ARTIFICIAL HEART IS NOT EXPECTED OR INTENDED TO PROVIDE A CURE FOR ALL HEART DISEASE. ULTIMATELY, AT BEST, IT IS EXPECTED [illegible] ONLY ONE PART OF A BROAD, MULTIFACITED SOLUTION TO THE PROBLEM. YET IN 1985 THE ARTIFICIAL HEART HAS BECOME THE MOST WIDELY PUBLICIZED DEVELOPMENT IN CARDIOVASCULAR MEDICINE.

PLEASE UNDERSTAND OUR GOALS. ALTHOUGH THE ARTIFICIAL HEART IS ONLY ONE OF MANY NEW APPROACHES, WHICH WHEN TAKEN TOGETHER MAY COMBINE TO DRAMATICALLY REDUCE THE TOLL OF HEART DISEASE, IT HAS BEEN JUDGED TO HAVE THE POTENTIAL TO SAVE AS MANY AS 50,000 LIVES PER YEAR. THUS, THE PRIMARY GOAL OF SYMBION'S RESEARCH IS TO HELP DEVELOP THE KNOWLEDGE NECESSARY TO ULTIMATELY PROVIDE A SAFE AND PRACTICAL DEVICE TO MEET THE PUBLIC NEED. THE GOAL IN THIS STAGE OF THE RESEARCH IS NOT TO PROVE THAT THE JARVIK-7^R HEART IS ACCEPTABLE FOR WIDESPREAD PERMANENT USE. WE ARE NOT NOW APPLYING FOR PRE-MARKET APPROVAL. THIS IS AN EXPERIMENTAL PROGRAM, AND LIKE A PHASE I DRUG STUDY, IT IS INTENDED TO EXPAND THE BASE OF OUR MEDICAL AND SCIENTIFIC KNOWLEDGE.

THE SCIENTIFIC STUDIES CONDUCTED UNDER OUR INVESTIGATIONAL DEVICE EXEMPTION HAVE BEEN DESIGNED PRIMARILY TO GENERATE AND EVALUATE CRUCIAL DATA WHICH CAN ONLY BE OBTAINED IN HUMANS AND FOR WHICH NO ACCEPTABLE ANIMAL MODELS ARE AVAILABLE. ALTHOUGH THE PROGRAM HAS GENERATED INTENSE HUMAN INTEREST, AND WE HAVE HELD THE WELL BEING OF EACH PATIENT AS A CRITICAL PRIORITY, WE WOULD NOT CONDUCT THESE STUDIES WITHOUT A WELL FOUNDED SCIENTIFIC APPROACH AND WITHOUT CLEAR SPECIFIC GOALS IN MIND.

THE MOST IMPORTANT QUESTIONS TO BE INVESTIGATED CONCERN THE LONG TERM INTERACTIONS OF THE DEVICE WITH THE HUMAN CIRCULATORY SYSTEM. INCLUDED AMONG THE INFORMATION WE HOPE TO LEARN ARE ANSWERS TO THE FOLLOWING:

DO THE METHODS WHICH PERMIT SUCCESSFUL SURGICAL IMPLANTATION OF THE ARTIFICIAL HEART PROVIDE A STABLE JUNCTION BETWEEN THE ARTIFICIAL MATERIALS AND THE LIVING TISSUES? IS THE HEMODYNAMIC FUNCTION STABLE AND ADEQUATE TO SUPPORT GOOD HEALTH. DOES THE PUMPING MECHANISM DAMAGE THE BLOOD ELEMENTS? WHAT ARE THE SPECIFIC ELEMENTS, IF ANY, OF THE DESIGN THAT COULD CREATE AN ENVIRONMENT CONDUCIVE TO THROMBUS FORMATION, PANNUS FORMATION, CALCIFICATION, OR INFECTION? HOW CAN THESE BE IMPROVED? DOES THE ARTIFICIAL HEART DAMAGE OTHER ORGAN SYSTEMS INCLUDING THE LUNGS, LIVER, KIDNEYS, NERVOUS SYSTEM OR THE IMMUNE SYSTEM? HOW CAN WE PREVENT ANY SUCH DAMAGE? WHAT RANGE OF CARDIAC OUTPUT IS ADEQUATE FOR REST AND EXERCISE AND WHAT CONTROL MODES ARE EFFECTIVE? DOES THE PATIENT EXPERIENCE PAIN OR DISCOMFORT? DOES THE EXTERNAL DRIVE SYSTEM FUNCTION RELIABLY UNDER REALISTIC CONDITIONS OF HUMAN USE? WHAT EMERGENCY ALARM SYSTEMS AND BACK UP SYSTEMS ARE REQUIRED? ARE THERE ANY DETRIMENTAL EFFECTS OF THE ALTERNATE RIGHT/LEFT PUMPING MODE USED WITH THE PORTABLE DRIVER? IS AN EXTERNAL PORTABLE DRIVE SYSTEM ACCEPTABLE TO PATIENTS AND SUFFICIENT TO PROVIDE GOOD REHABILITATION OR DO THEY REQUIRE A "FULLY IMPLANTABLE SYSTEM?"

OTHER QUESTIONS OF IMPORTANCE ARE: WHAT ARE THE MAJOR REQUIREMENTS FOR GOOD MEDICAL MANAGEMENT OF HUMAN ARTIFICIAL HEART PATIENTS? WHAT ARE THE APPROPRIATE SELECTION CRITERIA OR CONTRAINDICATIONS? WHAT ARE THE MAJOR ELEMENTS OF SURGICAL AND POSTOPERATIVE CARE AND WHAT IS THEIR EFFECT ON LONG TERM RESULTS? WHAT IS THE APPROPRIATE ANTICOAGULATION REGIME, THE APPROPRIATE ANTIBIOTIC MANAGEMENT, THE APPROPRIATE HYGIENE AND CARE OF THE PERCUTANEOUS LEADS? WHAT ARE THE MAJOR PHYCHOLOGICAL REACTIONS OF PATIENTS LIVING WITH THE ARTIFICIAL HEART? DO PATIENTS EXPERIENCE EXCESSIVE STRESS OR ARE THEY CAPABLE OF ADEQUATELY ADAPTING TO DEPENDENCY ON THE DEVICE? CAN THEY EXPERIENCE A SENSE OF WELL BEING AND MOTIVATION TO CONTINUE PRODUCTIVE LIVES? IS THE PRODUCTION OF HORMONES BY THE NATURAL ATRIA NORMAL OR ABNORMAL AFTER THE CORONARY ARTERIES ARE SEVERED DURING IMPLANTATION OF THE DEVICE WHAT ARE THE EFFECTS OF CARDIOVASCULAR DRUGS ONCE THE HEART IS REMOVED? ARE THERE ANY UNANTICIPATED SIDE EFFECTS OR DEVICE COMPLICATIONS?

THESE ARE ONLY SOME OF NUMEROUS AND IMPORTANT SCIENTIFIC QUESTIONS UNDER STUDY. WE HAVE OBTAINED A WEALTH OF INFORMATION ABOUT THESE AREAS OF INTEREST AND THERE STILL IS A GREAT DEAL TO BE LEARNED. WE HAVE PRESENTED MUCH OF WHAT WE HAVE LEARNED IN THE SPECIAL STATUS REPORT WHICH FDA REQUESTED IN ADVANCE OF THE USUAL ANNUAL IDE REPORT. WE WILL PRESENT CONSIDERABLE MORE INFORMATION THIS AFTERNOON AND ARE PREPARED TO ANSWER WHATEVER QUESTIONS YOU MAY HAVE TO THE BEST OF OUR ABILITY.

THERE IS MUCH WE CAN AND WILL LEARN. IN VIEW OF THIS, THE ARTIFICIAL HEART STUDY SHOULD BE CONSIDERED IN THE CONTEXT OF RESEARCH AND DEVELOPMENT OF NEW MEDICAL TECHNOLOGIES AND THE BROADLY ACCEPTED ETHICAL PRINCIPLES APPLIED TO EXPERIMENTATION WITH HUMAN SUBJECTS. THE JARVIK-7 HEART WAS DEVELOPED ON THE BASIS OF MORE THAN 25 YEARS OF ANIMAL RESEARCH BEGUN BY DR. KOLFF AND DR. AKATSU AT THE CLEVELAND CLINIC IN 1957. MANY OF THE BASIC PRINCIPLES UTILIZED BY INVESTIGATORS TWO DECADES AGO HAVE BEEN RETAINED AND MANY HAVE BEEN REFINED. HUNDREDS OF EXPERIMENTAL ANIMALS HAVE BEEN STUDIED WITH NUMEROUS ARTIFICIAL HEART MODELS AND THERE IS EXTENSIVE LITERATURE IN THE FIELD. STUDIES WITH THE JARVIK-7 HEART AND ITS FORERUNNERS, THE JARVIK-5 HEART, THE JARVIK-3 HEART AND THE KWAN-GETT HEART WERE A MAJOR PART OF THE ARTIFICIAL HEART PROGRAM FUNDED BY THE NATIONAL INSTITUTES OF HEALTH. ALSO INCLUDED IN THAT PROGRAM WAS WORK ON THE JARVIK-7 ELECTROHYDRALIC LVAD FUNDED UNDER THE NIH TARGETED ARTIFICIAL HEART PROGRAM ESTABLISHED BY A SPECIFIC ACT OF CONGRESS IN 1964.

TO DATE, MORE THAN 250 JARVIK HEARTS HAVE BEEN IMPLANTED IN ANIMALS IN THE UNITED STATES, EUROPE, SOUTH AMERICA, AND JAPAN. THE LONGEST SURVIVAL OF ANY ANIMAL IN THE WORLD WITH AN IMPLANTED TOTAL ARTIFICIAL HEART WAS TEN MONTHS, OBTAINED WITH THE JARVIK-7 HEART AT THE UNIVERSITY OF UTAH.

THE DECISION TO BEGIN HUMAN INVESTIGATION WITH THE TOTAL ARTIFICIAL HEART WAS MADE AFTER YEARS OF THOUGHTFUL CONSIDERATION

OF THE SCIENTIFIC INFORMATION TO BE GAINED AND THE ETHICAL ISSUES ASSOCIATED WITH THE INITIAL HUMAN USE.

TO BEGIN WITH, THE HEART IS ONLY TO BE USED IN PERSONS FACING IMMINENT DEATH FROM END STAGE HEART DISEASE. PATIENTS MUST BE WITHIN THE CLASS IV FAILURE CRITERIA ESTABLISHED BY THE NEW YORK HEART ASSOCIATION. THIS MEANS THAT PATIENTS HAVE A UNIFORMLY FATAL END STAGE CONDITION, A FAR WORSE PROGNOSIS THAN MOST FORMS OF CANCER AND MANY OTHER HORRIBLE DISEASES, INCLUDING AIDS. PATIENTS IN CLASS IV ARE GENERALLY BEDRIDDEN, EXTREMELY WEAK, SHORT OF BREATH UPON SLIGHT EXERTION AND OFTEN IN CONSIDERABLE PAIN. THEIR QUALITY OF LIFE IS DISMAL. THE PROTOCOLS FOR IMPLANTATION OF THE JARVIK-7 HEART APPROVED BY THE INSTITUTIONAL REVIEW BOARDS OF EIGHT DIFFERENT U.S. MEDICAL CENTERS HAVE ALL LIMITED THE USE OF THE DEVICE ONLY TO PATIENTS IN CLASS IV FAILURE OR PATIENTS UNWEANABLE FROM THE HEART LUNG MACHINE WHO FACE IMMEDIATE DEATH WITHOUT IT. ADDITIONALLY, ALL PROTOCOLS HAVE STIPULATED THAT THE ARTIFICIAL HEART COULD BE USED ONLY WHEN A HEART TRANSPLANT WAS UNAVAILABLE DUE TO CERTAIN CONTRAINDICATIONS OR DUE TO THE INABILITY TO OBTAIN A DONOR HEART IN TIME.

IN ADDITION TO THIS, THE PROCESS OF OBTAINING INFORMED CONSENT HAS BEEN EXTENSIVE AND THROUGHLY REVIEWED. WE DO OUR VERY BEST TO FULLY INFORM PROSPECTIVE RECIPIENTS AND THEIR NEXT OF KIN OF ALL POSSIBLE RISKS, INCLUDING THOSE AFFECTING QUALITY OF LIFE. WHILE IT MAY BE IMPOSSIBLE FOR SOMEONE FACING IMMEDIATE

DEATH TO FULLY UNDERSTAND EVERYTHING, PATIENTS ARE NEVERTHELESS VERY WELL INFORMED.

THE RESEARCH, THEN, IS CONDUCTED WITH INFORMED, CONSENTING PATIENTS WHO FACE CERTAIN NEAR-TERM DEATH. FURTHERMORE, WE MAKE ONLY ONE PROMISE - TO DO THE BEST FOR THEM THAT WE POSSIBLY CAN UNDER THE CIRCUMSTANCES AND TO HOLD THEIR INTERESTS FOREMOST. WE DO NOT PROMISE A LONGER OR A BETTER LIFE. IN FACT, WE INFORM THEM THAT THEIR LIFE MAY BE SHORTENED.

TO DATE, EIGHT PATIENTS IN THIS CONDITION HAVE BEEN TREATED WITH THE JARVIK-7 HEART. THREE OF THESE WERE BRIDGE-TO-TRANSPLANT PATIENTS, TWO OF WHOM ARE AT HOME NOW AND ARE IN EXCELLENT CONDITION FOLLOWING SUCCESSFUL HEART TRANSPLANTS DONE BY DR. JACK COPELAND IN TUCSON AND DR. BARTLEY GRIFFITH IN PITTSBURGH. THE THIRD, WAS OPERATED ONLY TWO DAYS AGO BY DR. LYLE JOYCE IN MINNEAPOLIS AND IT IS EARLY IN HER POSTOPERATIVE COURSE. THE OTHER FIVE HAVE BEEN PERMANENT IMPLANT PATIENTS; DR. DEVRIES' FOUR CASES AND ONE BY DR. SEMB IN STOCKHOLM. THE AVERAGE SURVIVAL OF THESE INDIVIDUALS IS PRESENTLY SEVEN MONTHS. THE TWO SURVIVING PATIENTS AT HUMANA HAVE BOTH LIVED LONGER THAN ANY EXPERIMENTAL ANIMAL COULD BE SUSTAINED IN THREE DECADES OF RESEARCH. BILL SCHROEDER HAS BEEN ALIVE FOR MORE THAN A YEAR.

A GREAT DEAL OF PUBLIC ATTENTION HAS BEEN DRAWN TO THE COMPLICATION OF THROMBOEMBOLISM AND STROKE. THIS HAS OCCURRED IN FOUR OF THE EIGHT HEART RECIPIENTS. IT HAS BEEN CATASTROPHIC FOR TWO OF THE PATIENTS. THE STROKES WHICH HAVE OCCURRED IN THE

OTHER TWO PATIENTS HAVE BEEN MILD AND THEY HAVE RECOVERED IN A FEW DAYS. MURRAY HADEN IS COMPLETELY FREE OF ANY EVIDENCE OF THROMBOEMBOLISM, OR STROKE, OR OTHER NEUROLOGIC COMPLICATIONS TEN MONTHS AFTER IMPLANTATION OF THE HEART. LEIF STENBERG - WHO RECENTLY DIED FOLLOWING A BRAIN HEMORRHAGE - HAD MANY MONTHS OF LIFE WITH EXCELLENT IMPROVEMENT IN HIS CONDITION. HE FREQUENTLY LEFT THE HOSPITAL TO GO TO DINNER IN RESTAURANTS, OR TO THE PARK, OR FOR A RIDE IN HIS CAR. HE WAS ABLE TO WALKUP FIVE FLIGHTS OF STAIRS WITH THE PORTABLE DRIVE SYSTEM. HE GREATLY ENJOYED HIS LIFE WITH THE JARVIK-7 HEART AND USED THE PORTABLE SYSTEM EXTENSIVELY. HE PROVED TO ME, WITHOUT A DOUBT, THAT A HIGH QUALITY OF LIFE IS POSSIBLE.

OTHERS HAVE BEEN MORE OR LESS FORTUNATE AND I WANT TO EMPHASIZE THAT WE ARE NOT INSENSITIVE TO THE DIFFICULT TIMES SOME OF THE PATIENTS AND THEIR FAMILIES HAVE EXPERIENCED. I CARE DEEPLY ABOUT THEM AND I HAVE FORMED MANY LASTING FRIENDSHIPS WITH THEM. I CERTAINLY WISH THAT WE COULD HAVE DONE MORE. BUT IN VIEW OF THE SEVERITY OF THEIR DISEASE, AND IN THE CONTEXT OF THE HISTORY OF OTHER NEW MEDICAL DEVICES USED TO TREAT OTHER SERIOUS DISEASES, THE JARVIK-7 HEART HAS PERFORMED EXTRAORDINARILY WELL AND I AM VERY PROUD OF THAT. CONSIDER SOME OTHER EXAMPLES: THE FIRST FOURTEEN PATIENTS TREATED WITH THE ARTIFICIAL KIDNEY DIED WITHIN DAYS; THE FIRST TWENTY PATIENTS TREATED WITH THE INTRAORTIC BALLOON PUMP DIED WITHIN DAYS; AND IN THE FIRST NIH STUDY WITH LEFT VENTRICAL ASSIST DEVICES, 21 OF 22 PATIENTS DIED WITHIN TWO WEEKS. HEART VALVES, PACEMAKERS AND ARTIFICIAL HIP

JOINTS HAD MANY PROBLEMS IN THEIR EARLY APPLICATIONS BUT TODAY THEY ARE COMMONPLACE AND EXTRAORDINARILY SUCCESSFUL.

PATIENTS WHO TAKE PART IN EARLY PHASE MEDICAL RESEARCH KNOW THAT THEY MAY NOT GAIN A LOT FOR THEMSELVES, BUT THAT THEIR CONTRIBUTION TO MEDICAL SCIENCE CAN BENEFIT OTHERS ENORMOUSLY. BARNEY CLARK WAS SUCH A MAN. BILL SCHROEDER, MURRAY HADEN, LEIF STENBERG, AND JACK BURCHAM HAVE ALL SAID THAT HELPING OTHERS WAS EXTREMELY IMPORTANT TO THEM. THEY HAVE HELPED AND WHAT WE ARE LEARNING WILL MAKE A DIFFERENCE.

I WOULD LIKE TO MAKE ONE FINAL COMMENT. EACH IMPLANT PATIENT HAS FACED A LIFE OR DEATH DECISION, WITH AN UNKNOWN FUTURE, AND WITH AN UNPREDICTABLE OUTCOME. BUT EACH HAS KNOWN THAT ONCE THE SURGERY WAS COMPLETED, A DEDICATED AND CAPABLE TEAM OF MEDICAL SPECIALISTS WOULD STAND BEHIND HIM, AND CARE FOR HIM FOR THE REST OF HIS LIFE. THE UTAH TEAM, THE HUMANA TEAM AND THE KOROLINKSA TEAM HAVE ALL DONE SO, AND HAVE ALL DEMONSTRATED AN EXTRAORDINARY COMMITTMENT TO SCIENCE AND HUMANITY. SYMBION IS PROUD TO WORK TOGETHER WITH THEM. WE REMAIN DEDICATED TO THE CONTINUATION AND ADVANCEMENT OF KNOWLEDGE THAT WILL LEAD TO THE DEVELOPMENT OF A PRACTICAL ARTIFICIAL HEART. DR. DEVRIES AND I LOOK FORWARD TO THE SESSION THIS AFTERNOON DURING WHICH WE PLAN TO EXPLORE IN AS MUCH DEPTH AS TIME WILL ALLOW WHAT WE HAVE LEARNED AND WHAT WE HOPE TO LEARN IN THE FUTURE. THANK YOU.

4160-01

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

[DOCKET NO. 85D-0291]

GUIDANCE FOR THE EMERGENCY USE OF UNAPPROVED MEDICAL DEVICES; AVAILABILITY

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing guidance, developed by FDA's Center for Devices and Radiological Health (CDRH), with respect to those emergency situations in which the agency would not object to a physician's using a potentially life-saving medical device for a use for which the device ordinarily is required to have, but does not have, an approved application for premarket approval or an investigational device exemption. The guidance is contained in a document entitled "Guidance for the Emergency Use of Unapproved Medical Devices."

DATE: Comments by (insert date 60 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Requests for single copies of the guidance document should be sent to Tracy A. Summers, Center for Devices and Radiological Health (HFZ-84), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

85-387

FOR FURTHER INFORMATION CONTACT:

Halyna Breslawec,
Center for Devices and Radiological Health (HFZ-403),
Food and Drug Administration,
8757 Georgia Ave.,
Silver Spring, MD 20910,
301-427-8162.

SUPPLEMENTARY INFORMATION: FDA is making available for comment guidance concerning the emergency use of an unapproved medical device. For the purpose of the guidance, an unapproved medical device is a device which, under section 501(f) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 351(f)), is subject to premarket approval to provide reasonable assurance of its safety and effectiveness for the purpose, condition, or use for which it is intended but which does not have in effect for such purpose, condition, or use either (1) a premarket approval application (PMA) under section 515 of the act (21 U.S.C. 360e) or (2) an Application for an Investigational Device Exemption (IDE) under section 520(g) of the act (21 U.S.C. 360j(g)) and Part 812 of FDA's regulations (21 CFR Part 812). In short, an unapproved device is a device that is utilized for a purpose, condition, or use for which the device ordinarily is required to have, but does not have, an approved PMA or IDE.

The guidance also concerns the emergency use by a physician of a device that is the subject of an approved IDE when the physician (i) is an investigator for the sponsor of the approved application but does not use the device in accordance with the terms and conditions of the application or (ii) is not an investigator.

An unapproved medical device may be used in human subjects only if it is approved for investigational use under an IDE and is used by an investigator for the sponsor in accordance with the terms and conditions of the application. IDE applications are reviewed by FDA promptly, and are deemed approved 30 days after their receipt by FDA, unless FDA notifies the sponsor that the investigation may not begin. FDA recognizes, however, that during the early phases of device design, development, and testing, an emergency may arise where, in a physician's judgment, an unapproved device would offer the only alternative for saving the life of a dying patient. Such a situation occurred recently with the use of an artificial heart. Realizing that there is a need for guidance on the use of unapproved devices in similar situations, CDRH developed a document that provides guidance to the physician with respect to emergency situations that require the use of such devices.

The guidance document discusses: (1) the criteria necessary for a situation to be considered an emergency; (2) the patient protection procedures the physician should follow before using an unapproved device in an emergency situation; (3) the procedures the physician should follow after using an unapproved device in an emergency situation; and (4) the situations in which use of an unapproved medical device is not justified, even though an emergency exists. The document also provides guidance to the sponsor of an approved IDE when the device that is the subject of the approved application is used in an emergency by a physician who is an investigator for the sponsor but who does not use the device in accordance with the terms and conditions of the application, or by a physician who is not an investigator. Finally, the document provides guidance to the physician in either of those circumstances.

FDA expects physicians to make the determination as to whether the criteria for emergency use of an unapproved medical device set forth in the guidance have been met. FDA will consider taking regulatory action if an unapproved device is used in inappropriate situations.

For the convenience of interested persons, FDA is including in this notice the entire guidance document:

Guidance for the Emergency Use of Unapproved Medical Devices

This guidance applies to the emergency use of an unapproved medical device. For the purpose of the guidance, an unapproved medical device is a device that is utilized for a purpose, condition, or use for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e) or an approved Application for an Investigational Device Exemption (IDE) under section 520(g) of the act (21 U.S.C. 360j(g)) and Part 812 of FDA's regulations (21 CFR Part 812).

An unapproved device may be used in human subjects only if it is approved for clinical testing under an IDE. An emergency need to use an unapproved device may occur when an IDE for the device does not exist, when a physician wants to use the device in a way not approved under the IDE, or when a physician or institution is not approved under the IDE.

In an orderly developmental process, the device's developer--a physician, scientist, or manufacturer--anticipates the need to conduct clinical studies and uses the IDE to ensure that adequate preclinical testing has been done, that the appropriate subjects will be selected, that subjects participate only after providing informed consent, that the device will be used properly, that subjects will be monitored adequately after the device is used, and that complete scientific data will be collected promptly. These data form the basis for subsequent marketing approval of the device.

The Food and Drug Administration (FDA) recognizes that even during the earliest phases of device design, development, and testing, emergencies arise where an unapproved device offers the only alternative for saving the life of a dying patient, but an IDE has not yet been approved for the device or the use, or an IDE has been approved but the physician who wishes to use the device is not an investigator under the IDE. Using its enforcement discretion, FDA will not object if a physician chooses to use an unapproved device in such an emergency, provided that the physician later justifies to FDA that an emergency actually existed.

Each of the following conditions should exist for a situation to be considered an emergency:

1. The patient is in a life-threatening condition that needs immediate treatment;
2. No generally acceptable alternative for treating the patient is available; and
3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects the physician to determine whether these criteria have been met, to assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist. FDA further expects the physician not to conclude that an "emergency" situation exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than remains. Physicians should be aware that FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.

In the event that a device is used in circumstances meeting the criteria listed above, FDA would expect the physician to follow as many patient protection procedures as possible. These include obtaining:

1. An independent assessment by an uninvolved physician;
2. Informed consent from the patient or a legal representative;
3. Institutional clearance as specified by institutional policies;
4. The Institutional Review Board (IRB) chairperson's concurrence; and
5. Authorization from the sponsor, if an approved IDE for the device exists.

FDA would not object if an unapproved device were shipped without FDA approval to a physician who claims to be faced with, and describes, the kind of emergency situation discussed above. The person shipping the device should notify FDA--by telephone (301-427-8162)--immediately after shipment is made. An unapproved device may not be shipped in anticipation of an emergency.

After an unapproved device is used in an emergency, the physician should:

1. Notify the IRB and otherwise comply with provisions of the IRB regulations (21 CFR Part 56) and the informed consent regulations (21 CFR Part 50);

2. Evaluate the likelihood of a similar need for the device in the future: If it is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for the device's subsequent use;

3. If an IDE exists, notify the sponsor of the emergency use of the device. The sponsor must comply with the reporting requirements of the IDE regulations; and

4. If an IDE does not exist, notify FDA of the emergency use of the device and provide FDA with a written summary of the conditions constituting the emergency, patient protection measures, and any scientific results.

Subsequent use of the device in an emergency situation may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been

> filed with FDA and FDA disapproves the IDE application, the device may not be used even if the circumstances constituting an emergency exist. Developers of devices that could be used in emergencies should anticipate the likelihood of emergency uses and should obtain an approved IDE. FDA will consider taking regulatory action if an unapproved device is used in inappropriate situations.

CDRH developed this guidance in response to a situation concerning the emergency use of an unapproved cardiovascular device. CDRH will apply this guidance to other types of potentially life-saving unapproved devices in emergency situations. In all situations in which the use of an unapproved device would not meet the criteria for emergency use under this guidance, such unapproved device may not be used without an approved IDE.

Interested persons may, on or before (insert date 60 days after date of publication in the FEDERAL REGISTER), submit written comments to the Dockets Management Branch (address above). Two copies of any comments should be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. FDA will consider any comments received. The document and comments received may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: October 12, 1985

OCT 12 1985

Frank E Young

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

Jacquelyn L Price

symbion, inc.
825 North 300 West • Salt Lake City, Utah 84103 • (801) 531-7022 • Telex 453-230 • Fax 801 531 6296

December 23, 1985

Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 4-62
5600 Fishers Lane
Rockville, Maryland 20857

RE: Docket No. 85D-0291
Guidance For The Emergency Use of Unapproved Medical Devices

To whom it may concern:

I would like to comment on FDA's proposed "Guidance for the Emergency Use of Unapproved Medical Devices" that the FDA published for comment on October 12, 1985. 50 Fed Reg. 42866. This letter represents my views as a scientist, a physician, and as an individual experienced in dealing with many of the practical realities, difficulties and policy issues associated with the initial human use of the total artificial heart.

In my work with the University of Utah and with Symbion, Inc. (both in the United States and abroad), I have never participated in any decision that resulted in the selection of an individual patient who was to be treated with an artificial heart. However, as President of Symbion, on four occasions I have had to refuse to aide physicians who called me requesting emergency permission to use the JARVIK-7® total artificial heart in desperate circumstances. In these cases, each patient was either unweanable from cardiopulmonary bypass, or temporarily on an external circulatory support device, or considered not to be a transplant candidate. All four were rapidly deteriorating. Each of these patients died shortly after my permission to use the JARVIK-7 heart was denied.

There were several reasons for refusing assistance. Foremost, was the fact that the clinical teams were not trained in the use of the total artificial heart and its support systems. In addition, there would have been an unavoidably long delay in transporting the equipment to the user, setting it up, and testing it. In view of this, I believe there was no reasonable chance of saving the patients' lives.

In my view, an emergency medical procedure only should be undertaken when, in the physician's judgment, there is a reasonable possibility of success. If an unapproved medical device is involved, I believe, among other conditions, it is appropriate for the FDA to ensure that the physicians either have sufficient direct knowledge of the application of the device or have the assistance of others who possess such knowledge.

The investigational device exemption (IDE) process requires careful sponsor preparation and FDA review of an application for the new device or for a new use of an existing device. Unfortunately, the IDE application process is ridged and can be lengthy and it was not designed to take into account the occasional need to use a potentially life saving device in emergency situations. For this reason, I commend FDA for proposing guidelines to permit emergency use of potentially life saving devices when no IDE has yet been approved. However, in my opinion, the proposed guidelines should be more broadly structured to more closely reflect actual medical needs. Further, the guidelines for emergency use of unapproved devices should differentiate situations in which the physician and medical team are experienced in the use of the device from situations in which they are not. I believe the following distinctions may be helpful:

1. If the physician and available support personnel or consultants have had no experience with the device in question, emergency use should not be permitted unless the device is substantially equivalent to another device with which they have had sufficient experience.

2. If the physician and appropriate team members have been sufficiently trained in the use of the device, and in their professional judgment no alternative is available, the emergency use should be permitted so long as both Institutional Review Board approval and patient consent have been obtained and an IDE has been filed with FDA.

The proposed guidelines currently state, "Physicians should be aware that FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impractical." the October 12th proposal further states, "Developers of devices that could be used in emergencies should anticipate the likelihood of emergency uses and should obtain an approved IDE." In my opinion, it is not always possible to satisfy these conditions. It is inevitable in almost every situation associated with potentially life-saving devices for which no alternatives exist that a medical emergency may arise after an IDE has been submitted but while it still is under review by the FDA. This places the physician, the patient, the sponsor, and the FDA in an ethically and legally untenable position. FDA's emergency use policy, as presently drafted, would require the medical team to allow the patient to die or to use the unapproved device and run the risk of FDA sanctions. In the process of seeking an approved IDE there always will be a period of time in which both the developer(s) and the Institutional Review Board concur that the device, the team, and the protocol are complete and satisfactory. According to FDA, between this time and the completion of FDA review, if an emergency arises, even if all the conditions in the proposed guidelines are met, the device could only be used once.

This is an arbitrary and medically inappropriate distinction. There is no reason to allow the patient whose emergency arises first to live while the next patient or patients must die simply because their crisis arose at a subsequent time and IDE review had not been completed. Life or death decisions should not turn on serendipitous factors such as when a crisis arises and how rapidly a physician can contact a sponsor to seek permission to be the first and only user as of a not yet approved device. If FDA policy requires the sponsor to deny a subsequent use of the device, both FDA and the sponsor will be subjected to unwarranted and severe criticism. I believe the better policy, and one that FDA can lawfully support, is to not to limit emergency device use to one time only situations.

As a related point, the proposal specifically states "An approved device may not be shipped in anticipation of an emergency." Therefore, the draft guidelines virtually assure that there will be a delay while a physician requests, and the sponsor arranges for, shipment of the devices. This delay may very substantially decrease the likelihood of success from medical treatment.

In my opinion, it is inappropriate for the FDA to publish guidelines that define a situation in which an unapproved device may be used in an emergency, while at the same time those guidelines contain provisions that make use of that device significantly less likely to succeed and that arbitrarily limit such use to one time only. Either the guidelines should strictly prohibit emergency use or they should be drawn to maximize the opportunity for success in appropriate emergency situations and thus truly protect the public and the patient.

I concur with the requirement that the FDA be notified of the emergency use of the device and that the FDA be provided with a written summary of the conditions constituting the emergency and with the details regarding patient protection and scientific results. I further concur with the manner in which an emergency is defined and with the obligations imposed on a physician to determine that the emergency use criteria have been met.

If the FDA were to change the guidelines and permit a medical team that has Institutional Review Board approval to maintain the equipment on site in readiness, and to proceed with emergency use during the period of time the IDE application was under FDA review, I believe a consistent FDA position could be achieved where patients facing otherwise certain death would have the best medical care available. The FDA would not mandate dangerous and harmful delays, and the physician would not be placed in the "catch-22" situation of either treating his/her patient less than opitimally or letting the patient die. I do not believe this would constitute a regulatory loophole of any serious magnitude that would be used to circumvent the Medical Device Ammendments to the Federal Food, Drug, and Cosmetic Act. The Institutional Review Board process would be fully utilized and, in the event that the FDA felt the emergency use in general or at any given institution was inappropriate, the Agency could immediately disapprove the investigational device exemption application for that institution or for that use.

In this regard, I believe a distinction can be drawn between outright denial of an IDE and a letter from FDA stating that an IDE is "not approvable" pending submission of additional information. In the former situation, the device could not be used in an emergency, while in the letter it could be used so long as the requested information was being developed for submission to FDA.

I sincerely urge you to modify the proposed guidelines to reflect these suggestions and to resolve the dilemma they would create if not changed. I believe that an appropriate balance of the interests of the public, the FDA, the device developer, the institution involved, the individual physician, and the dying patient can be found. I would be pleased, based on my practical experience with emergency use situations, to work with the Agency to further define useful and workable conditions for emergency use.

Yours truly,

Robert Jarvik M.D.
President
Symbion, Inc.

cc: John Villforth
Frank E. Young, M.D. Ph.D.
Frederick Bowen, M.D.

symbion, inc.

825 North 300 West • Salt Lake City, Utah 84103 • (801) 531-7022 • Telex 453-230 • Fax 801 531 6296

January 6, 1986

Dr. Jack G. Copeland
Professor & Chief
Cardiovascular & Thorcic Surgery
University of Arizona, Health Sciences Center
1501 North Campbell Ave., Room 4402
Tucson, AZ 85721

Dear Jack:

On October 12, 1985 the Food and Drug Administration issued a document entitled "Guidance for the Emergency Use of Unapproved Medical Devices". On December 19, 1985 Dr. Lyle Joyce implanted the 70cc JARVIK-7® total artificial heart as a bridge to transplant in Mary Lund. At the present time she is making steady progress and I am hopeful that she will become a transplant candidate in the near future.

On January 1, 1986, Symbion received a letter from the FDA indicating that under the emergency use guidelines, the FDA requires that there be no more implantations of the 70cc JARVIK-7 heart until it has been approved by the FDA for investigation. Based on this, it now appears that Symbion cannot provide the 70cc heart to any physician for emergency use without the prior consent of FDA.

On December 23, 1985 I sent a letter to the FDA in response to their solicitation of comments on FDA's proposed "Guidance for the Emergency Use of Unapproved Medical Devices". In that letter, Symbion recommended that emergency use should be permitted after a medical team had obtained IRB approval during the time the application for an investigational device exemption was under review by the FDA. I am hopeful that the FDA will adopt such a policy. Although they have not yet done so, I understand that a true emergency situation may arise in which you believe you may be able to save the life of a patient utilizing the small JARVIK-7 heart. I have every confidence that this device is safe and effective and appropriate to use in such a case if the FDA will grant approval.

If an emergency situation arises and you call Symbion to request the small JARVIK-7 heart our position is a follows: If we concur that it is an appropriate case, we will immediately send a Symbion representative to the Texas Heart Institute with two sterile small JARVIK-7 hearts. If FDA grants you verbal approval to implant the heart in an emergency attempt to save your patients life, our representative will deliver the hearts to you. However, we will retain the hearts in our possession and will not deliver them to you without FDA's approval.

I know that this situation is certainly less than optimal and could cause a delay that would result in serious complications for the patient. I certainly believe it would be much better to have the heart sterile in your hospital on stand-by, but unfortunately the FDA presently will not permit that. Also, I hope you will understand that we must abide by the law and while doing so, do what we feel is right to provide at least some opportunity to treat patients in emergency need.

Yours truly,

Robert Jarvik, M.D.
President

tw

Enclosures:

1. FDA Document - Guidance for the Emergency Use of Unapproved Medical Devices - October 12, 1985

2. Jarvik letter to FDA - December 23, 1985

3. FDA letter of December 31, 1985

TOTAL ARTIFICIAL HEART
IDE Supplements and Correspondence

TO: FDA/ Dr. Joe Hackett
Bureau of Medical Devices

FROM: Kolff Medical/Lee M. Smith, Ph. D.

DATE: July 14, 1980

RE: Copy of IDE Application being considered by the University of Utah Human Experimentation Committee. Notification will be made at time of approval.

(Approximately 50 pges)

TO: Kolff Medical/Lee M. Smith, Ph. D.

FROM: FDA/Michael J. Andrews, Ph. D.

DATE: July 31, 1980

RE: Resubmission of IDE Application after IRB approval.
(Approximately 55 pages)

TO: FDA/Document Control Center

FROM: Kolff Medical/Lee M. Smith, Ph. D.

DATE: February 27, 1981

RE: **IDE APPLICATION - "Total Heart Replacement in Man"**
Principal Investigator - William C. DeVries, M.D.
University of Utah Medical Center,
Salt Lake City, Utah
(Approximately 100 pages)

TO: Kolff Medical/Lee Smith

FROM: FDA/Jeanne C. McDowell - Document Control Center

DATE: March 30, 1981

RE: **Assignment of IDE NUMBER - G810057**
Total Heart Replacement in Man

TO: Kolff Medical/Lee M. Smith, Ph. D.

FROM: FDA/Victor Zafra, Bureau of Medical Devices

DATE: March 24, 1981

RE: **FDA's response to IDE Application for TAH - U of U**
Deficiencies included:

1) Patient Protocol
2) Patient Consent Form - lack of Data
3) Lack of scientific Protocols to assess the adequacy of cardiac output, etc.

Six pages of attached questions including Device Description, In Vitro Testing, Animal Testing, Manufacturing/Quality Control, IRB Membership, Clinical Investigation, Consent Form, Scientific Protocol, Hospital Use and Post-Hospital Use.

TO: FDA/Document Control Center

FROM: Kolff Medical/Lee M. Smith, Ph. D.

DATE: August 5, 1981

RE: Total Artificial Heart - IDE #G810057

Response to FDA's Panel questions concerning the IDE Application for the clinical use of the total artificial heart.
(Approximately 230 pages)

TO: Kolff Medical/Lee M. Smith, Ph. D.

FROM: FDA/Victor Zafrz

DATE: September 10, 1981

RE: **APPROVAL OF IDE APPLICATION G810057/A1**
Approval-with Patient Consent Form Modifications.
Approval for seven (7) implants at University of Utah.

(Also included are consultants concerns regarding-
1) Age of candidate,
2) Inability to defibrillate as a criteria,
3) Manual rather than automatic switching system for back-up unit of drive unit.
4) Need for documentation of specific organisms that cause infection.

NOTE: **ANY MANUFACTURING CHANGE MUST BE SUBMITTED AND APPROVED BY FDA THROUGH A SUPPLEMENTAL APPLICATION BEFORE IT IS ADOPTED.**

TO: FDA/ Michael Andrews

FROM: Kolff Medical/Lee Smith, Ph. D.

DATE: November 4, 1981

RE: Exportation of Total Artificial Heart

TO: FDA/Bureau of Medical Devices, G. Rahmoeller

FROM: Kolff Medical/Lee M. Smith, Ph. D.

DATE: December 8, 1981

RE: **Total Heart Replacement in Man - IDE #G810057 S/1**

Revised Patient Consent Form (per FDA request of 9/10/81.

(Approximately 10 pages)

TO: Kolff Medical/Lee M. Smith, Ph. D.

FROM: FDA/ Victor Zafra - Acting Director

DATE: February 12, 1982

RE: **Total Artificial Heart - IDE #G810057 S1, S2 and S3**

Approval of supplements correcting Patient Consent Forms.
Final Approval for beginning of Investigation of Total
Artificial Heart in Man,
University of Utah,
William C. DeVries, M.D.

TO: FDA/Glenn Rahmoeller

FROM: Kolff Medical/Lee Smith, Ph. D.

DATE: March 11, 1982

RE: **Partnership formation**
Robert Jarvik, M.D.
374 West 600 North,
Salt Lake City, Utah.

TO: Kolff Medical/Lee M. Smith, Ph. D.

FROM: FDA/Victor Zafra

DATE: April 8, 1982

RE: **Total Artificial Heart, IDE #G810057/S4**

Approval of Kolff Medical as Sponsor of the Investigation under new partnership.

TO: FDA/Glenn Rahmoeller

FROM: Kolff Medical/Lee M. Smith, Ph. D.

DATE: May 24, 1982

RE: **Total Artificial Heart - IDE #G810057**

DRAFT of proposed expanded protocol for artificial heart recipients.

(Approximately 22 pages)

TO: FDA/Glenn Rahmoeller

FROM: Kolff Medical/Lee M. Smith, Ph.D.

DATE: May 26, 1982

RE: **Total Artificial Heart - IDE #G810057/S5**

Amendments to the Total Artificial Heart Patient Selection Criteria. (Approved by University of Utah IRB)

(Approximately 12 pages)

TOTAL ARTIFICIAL HEART
IDE #G810057
March 1983 -

TO: FDA/Bill Letzing - Bureau of Medical Devices

FROM: Kolff Medical/Bill Moeller

DATE: March 1, 1983

RE: Letter regarding summary data on all artificial heart valves from manufacturers.

TO: MEMO

FROM: William C. Moeller

DATE: March 7, 1983

RE: **FDA visit of February 28, 1983 - March 1, 1983**

Summary of notes written by Dr. Glenn Rahmoeller.
Subjects covered:

1) Barney Clark - Revised protocol and results of fractured heart valve.
2) Next Patient - Revised protocol regarding Patient Selection Criteria, review data concerning heart valves, number of patients that can be handled at the same time and overall plan for seven patients.
3) Future - overall plan for IDE and PMA, expansion of IDE for additional centers and plan for PMA centers.

(3 pages)

TO: Dr. Kolff

FROM: Robert Jarvik, M.D.

DATE: March 9th, 1983

RE: Summary of FDA recommendations after visit from Bill Letzing and Glenn Rahmoeller.

TO: University of Utah IRB (no indication of IDE Submission)

FROM: William C. DeVries/Kolff Medical

DATE: March 8, 1983

RE: **Total Artificial Heart - IDE #G81057**

Supplement application for use of the Portable Drive System in Human Patients.

(Approximately 35 pages)

TO: FDA/ Robert G. Britain

FROM: Kolff Medical/P. Elaine Duncan

DATE: May 3, 1983

RE: **Total Artificial Heart - IDE #G810057/A1-S5**

Notification of Incorporation -
Kolff Medical, Inc.
374 West 600 North
Salt Lake City, Utah 84103

TO: Kolff Medical/P. Elaine Duncan

FROM: FDA/Robert G. Britain

DATE: July 21, 1983

RE: Total Artificial Heart - IDE #G810057/ S6

Approval of placement of IDE #G810057 under new corporation.

TO: MINUTES FROM:

CIRCULATORY SYSTEM DEVICES ADVISORY PANEL
(Closed Session)
Washington, D. C.

DATE: Friday, June 24, 1983

RE: Total Artificial Heart - IDE #G810057

Presentation by Robert Jarvik, M.D. regarding Barney Clark and Kolff Medical plans for the future.

TO: FDA

FROM: William DeVries, M.D.

DATE: August 26, 1983

RE: JARVIK-7® total artificial haert
University of Utah

Amendment to include additional group of potential patients under the selection criteria. Dr. DeVries adds HEIMES™ driver protocol and removes eight week waiting period.

TO: FDA

FROM: Humana Audubon/William C. DeVries, M.D.

DATE: November 24, 1983

RE: Total Artificial Heart in Man - Protocol

Revised protocol and appendices. University of Utah Informed Consent - (17 pages)

(Approximately 175 pages)

TO: FDA/Glenn Rahmoeller

FROM: Kolff Medical/E. Duncan

DATE: January 20, 1984

RE: **JARVIK-7® total artificial heart**
IDE Supplement G810057/S7, University of Utah

1) Summary of First Case and Review Process.

2) Valves: Analysis of Failure and Choice of Medtronic.

3) Revised Protocol and Informed Consent.

4) Devices: Additions and Amended Descriptions

(Approximately 370 pages)

TO: FDA/Glen Rahmoeller
FROM: W. Moeller/Kolff Medical
DATE: February 1, 1984
RE: Photographs and video requested

TO: Kolff Medical/E. Duncan
FROM: DFA/Robert G. Britain
DATE: March 14, 1984
RE: Total Artificial Heart - IDE G810057/S8

FDA Response to IDE Application of January 20th, 1984. Non approvable due to additional data and four pages of deficiencies.

TO: FDA/Robert G. Britain
FROM: Kolff Medical/R. Jarvik & E. Duncan
DATE: April 23, 1984
RE: Response to FDA's letter of March 14, 1984 regarding IDE Application Total Artificial Heart.

1) Addition information on valve modification.
2) Clarification of certain experiences with first human case.
3) Clarification of and expansion on relevant data and clinical investigation plan for HEIMES™ portable driver.
4) Clarification of the deliberation of the U of Utah IRB in the review of first human case and revised protocol.

(Approximately 175 pages)

TO: FDA/Glen Rahmoeller

FROM: Kolff Medical/Robert Jarvik, M.D.

DATE: June 5, 1984

RE: IDE SUPPLEMENT - G810057/S9 OF APRIL 23, 1984
Additional information as an appendix to IDE Supplement.

1) Description of Improvements in Manufacturing and Q.C.
2) Documentation of Mock Loop Accuracy of Turbine Flow Meter.
3) Accuracy of Cardiac Output - COMDU™ Monitor
4) Alternate Left-Right Pumping
5) Clarification of Questions concerning Starling's Law
6) Explanation of conflicts in supplement document.

(Approximately 20 pages)

TO: FDA/G. Rahmoeller

FROM: Kolff Medical/R. Jarvik, M.D.

DATE: June 12, 1984

RE: IDE Application G810057/S9

Additional documentation - JARVIK-7 heart and mock circulation data demonstrating accuracy of HEIMES™ portable driver.

Also reference to recommendation that name of the corporation be changed - proposed name SYMBION.

TO: Kolff Medical/R. Jarvik, M.D.

FROM: FDA/R. Britain

DATE: June 18th, 1984

RE: **APPROVAL OF IDE APPLICATION G810057/S8,S9,S10 & S11**
University of Utah Medical Center
Salt Lake City, Utah.

TO: FDA/Glen Rahmoeller

FROM: SYMBION, INC./ Robert K. Jarvik, M.D.

DATE: September 19, 1984

RE: Request for Supplement Approval to add Humana Hospital Audubon as Implant Center under IDE Approval of William DeVries, M.D. as Clinical Investigator

Notification of formal name change to SYMBION, INC.

(Part I included all IDE Submission information for Humana Audubon and Part II included revised Protocol from Humana Hospital Audubon - total pages approx. 450.)

NOTE: Part II (Protocol: Total Artificial Heart in Man) dated September 13, 1984 as approved by Humana IRB)

TO: FDA/Glen Rahmoeller

FROM: SYMBION/R. Jarvik, M.D.

DATE: October 14, 1984

RE: IDE Supplement G810057/S12
Additional information and clarifications requested by Dr. Letzing at Humana Hospital Audubon. (Questions regarding IRB compliance, Protocol, backup equipment, substitution of Dr. Lansing as Co-Investigator, etc.)
(Approximately 20 pages)

TO: SYMBION/R. Jarvik, M.D.

FROM: FDA/ R. Britain

DATE: November 2, 1984

RE: **APPROVAL OF IDE SUPPLEMENT G810057/S12 AND S13**

Humana Hospital Audubon, Louisville, Kentucky.

TOTAL ARTIFICIAL HEART
IDE Supplements and Correspondence

DATE: April 12, 1985

RE: IDE Supplement to add Texas Heart Institute
("Implantation of a Temporary Total Artificial
Heart Prior to Cardiac Transplantation"
Bridge to transplant.

DATE: May 10, 1985

RE: FDA response to IDE Supplement dated 4/12/85
regarding Texas Heart Institute.

DATE: April 4, 1985

RE: IDE Supplement to add Abbott Northwestern Hospital.
Dr. Lyle Joyce. (Appendix A)

DATE: May 9, 1985

RE: FDA response to IDE Supplement dated 4/9/85
regarding Abbott Northwestern Hospital.

DATE: May 17, 1985

RE: Response to FDA letter of May 9, 1985 regarding
Abbott Northwestern Hospital.
- Exhibit I - Patient Consent Form.
- Exhibit II - VAD vs. TAH
- Exhibit III - Time period - Donor heart.
- Exhibit IV - Duration of use of TAH
- Exhibit V - Personnel trained in use of TAH
- Exhibit VI - IRB Committee
- Exhibit VII -IRB Assurance of Compliance Cert.

DATE: June 3, 1985

RE: IDE Supplement to add University of Arizona,
Jack G. Copeland, M.D.

DATE: June 3, 1985

RE: IDE Supplement to add University of Pittsburgh,
Dr. Bartley P. Griffith.

DATE: June 19, 1985

RE: FDA Response to IDE Supplement of May 17th,
Abbott Northwestern Hospital

DATE: June 28, 1985

RE: FDA Response to IDE Supplement of June 3, 1985
University of Arizona.

DATE: July 3, 1985

RE: Response to FDA Letter of June 19th regarding
addition of Abbott Northwestern Hospital.

DATE: July 5, 1985

RE: FDA Response to supplement of June 3, 1985 to
add University of Pittsburgh.

DATE: July 9, 1985

RE: Response to FDA letter of June 28th regarding
addition of University of Arizona - Dr. Copeland.

DATE: August 2, 1985

RE: FDA Response to IDE Supplement of July 3, 1985
regarding Abbott Northwestern Hospital - Dr. Joyce.
S19

DATE: August 7, 1985

RE: Response to FDA letter of July 5th, 1985 regarding University of Pittsburgh.

Exhibit I
Investigators training and experience
Members of Surgical team and their functions and responsibilities.

Exhibit II
Names and affiliation of each of the members of the IRB

Exhibit III
Letter for chairman of IRB

Exhibit IV
Informed Consent Form

DATE: August 13, 1985

RE: Response to FDA letter of August 2nd, 1985 regarding Abbott Northwestern Hospital Patient Consent Form. (Revised consent form dealing with all six of the questions raised by FDA.

DATE: August 16, 1985

RE: FDA Approval of University of Arizona, Dr. Jack Copeland. "Bridge to Transplant - G810057/S20.

TO: FDA/ Betty Lemperle

FROM: DFG

DATE: August 19, 1985

RE: Response to FDA questions on July IDE Supplement S17 - University of Pittsburgh, Dr. Bartley Griffith
Training of clinical team and identification of surgical staff.

TO: Symbion/DFG

FROM: FDA/Britain

DATE: August 22, 1985

RE: Approval of IDE G810057/S22 and 24
University of Pittsburgh, Dr. Bartley Griffith
"Bridge to Transplant"

TO: Symbion/DFG

FROM: FDA/Britain

DATE: August 30, 1985

RE: Approval of IDE G810057/S23
Abbott Northwestern Hospital, Dr. Lyle Joyce
"Bridge to Transplant"

TO: Symbion/RKJ

FROM: FDA/Britain

DATE: September 5, 1985

RE: **"Bridge to Transplant"**
Reference to meeting with DFG in D.C. regarding submission of separate IDE Submission and protocol for "Bridge to Transplant and written description of perceived scope of investigation and potential number of institutions.

TO: DFA/ Document Mail Center

FROM: DFG/Symbion

DATE: September 10, 1985

RE: Response to FDA letter of May 10, 1985 re: IDE Submission adding Texas Heart Institute, Dr. Frazier

Exhibit I	Informed Consent
Exhibit II	Letter of IRB Chairperson
Exhibit III	Members of clinical team
Exhibit IV	Clinical Training of team and back-up equipment
Exhibit V	IRB members- Background and affiliation

TO: FDA/Document Mail Center (cc: Acharya and Letzing)

FROM: DFG/Symbion

DATE: September 24, 1985

RE: **PATIENT REPORT** - IDE G810057/S12 S13
William C. DeVries - U of U and Humana Audubon

Patient Summary from U of Arizona, Dr. Jack Copeland

Also reference to permanent use by Abbott Northwestern, Dr. Lyle Joyce.

TO: FDA/Document Mail Center (cc: B. Lemperle)

FROM: DFG/Symbion

DATE: September 30, 1985

RE: IDE SUPPLEMENT - **"Bridge to Transplant"**
St. Luke's Hospital - Milwaukee, Wisconsin
Dr. Alfred Tector

Exhibit I	List of those trained in TAH program and their background and training.
Exhibit II	IRB members and affiliations
Exhibit III	IRB letter of approval
Exhibit IV	Patient consent form
Exhibit V	Team members and their responsibilities

TO: FDA/Document Mail Center (cc: B. Lemperle)

FROM: DFG/Symbion

DATE: October 3, 1985

RE: IDE Supplement **"Bridge to Transplant" and Permanent**
St. Luke's Medical Center, Phoenix, Arizona
Dr. Cecil C. Vaughn

Exhibit I	List of those trained in TAH program and extent of training.
Exhibit II	Clinical team and their responsibilities
Exhibit III	Additional clinical experience of Dr. Cecil Vaughn.
Exhibit IV	IRB members and their affiliations.
Exhibit V	IRB letter of approval
Exhibit VI	Patient consent form/"Bridge"
Exhibit VII	Patient consent form/Permanent

TO: DFG/Symbion
FROM: FDA/Kshitij Mohan
DATE: October 10, 1985
RE: IDE Supplement S27
Non-approval of Texas Heart Institute, Dr. Frazier
"Bridge to Transplant"

TO: DFG/Symbion
FROM: FDA/Kshitij Mohan
DATE: October 17th
RE: TAH - S29
Acknowledgement of Patient Progress Report

Reference to "any significant modifications to J-7 TAH", requirement of pre-clinical engineering and animal testing and need for FDA approval.

Denial of request to add Abbott Northwestern Hospital, Dr. Lyle Joyce as a Permanent Investigational site. "FDA will consider approval only after the first seven implants at Humana Audubon are completed and reviewed."

TO: FDA/Abhijit Acharya (cc: K. Mohan, W. Letzing)
FROM: DFG/Symbion
DATE: October 23, 1985
RE: Correspondence - **JARVIK-7 total artificial heart-70cc**
Reasons why Symbion does not believe an IDE supplement is necessary for the 70cc. Included comparative data between 70cc and 100cc TAH and description of 70cc.

TO: DFG/Symbion

FROM: FDA/Kshitij Mohan

DATE: October 25, 1985

RE: IDE Supplement - G810057/S31
St. Luke's Medical Center, Phoenix, Arizona
Dr. Tector - "**Bridge to Transplant**"
Denial of supplement.

FDA requirement of a new IDE Investigational plan for the short term use of the total artificial heart, including protocol, risk analysis, purpose of investigation, etc.

Denial of addition as permanent investigational site.

TO: DFG/Symbion

FROM: FDA/Kshitij Mohan

DATE: October 24, 1985

RE: **JARVIK-7 total artificial heart-70cc**

Dr. DeVries call to FDA regarding 70cc heart and approval as an IDE supplement.

Reference to phone conversations of October 18th and 21st regarding need for 70cc supplement and Emergency Use guidelines. Also shipment of 70cc to investigational site prior to Emergency Use. "....you must immediately withdraw all the unapproved devices shipped to any institutions or investigators.

TO: DFG/Symbion

FROM: FDA/Kshitij Mohan

DATE: October 29, 1985

RE: IDE Supplement S30 - "**Bridge to Transplant**"
Denial of supplement to add St. Luke's Hospital, Milwaukee, Wisconsin, Dr. Cecil Vaughn.

Reference to need for IDE Submission to add "Bridge", IDE supplement for 70cc, patient selection criteria for bridge to transplant and transplant candidacy.

TO: Jack Copeland, M.D./University of Arizona

FROM: FDA/Abhijit Acharya

DATE: October 31, 1985

RE: **JARVIK-7 total artificial heart - 70cc**
70cc not approved - prior shipment of unapproved device is not allowed and use of device will be in violation of FDA regulations.

TO: FDA/Kshitij Mohan

FROM: DFG/Symbion

DATE: November 8, 1985

RE: Correspondence/**JARVIK-7 total artificial heart - 70cc**

Response to FDA letter of October 24th, 1985. Notification of actions taken by Symbion: verbal and written notification to involved investigational sites regarding FDA's position on 70cc and Emergency Use Guidelines. Removal of 70cc hearts from all investigational sites.

TO: FDA/Document Mail Center

FROM: DFG/Symbion

DATE: November 8, 1985

RE: IDE Submission - **"BRIDGE TO TRANSPLANT"**
New Investigational Plan, protocol, patient consent form, patient selection criteria, data analysis, etc.

Reference also to supplemental IDE's for St. Luke's in Phoenix and Milwaukee (Vaughn and Tector).

Request "Umbrella Policy" for future bridge-to-transplant.

TO: DFG/Symbion

FROM: FDA/Halyna P. Breslawec

DATE: November 13, 1985

RE: IDE Document Control Number for **"Bridge to Transplant"**
IDE #G850204, Dated November 8, 1985

TO: DFG/Symbion

FROM: FDA/Keith Lusted(Circulatory Systems Devices Panel)

DATE: November 22, 1985

RE: Notification of Panel Meeting and Public Hearing

TO: DFG/Symbion

FROM: FDA/Kshitij Mohan

DATE: November 22, 1985

RE: IDE Supplement - **JARVIK-7 total artificial heart-70cc**
Denial of addition of 70cc. Request for IDE supplement.
Note: Even after FDA approval program may not be implemented until IRB approval is obtained and FDA has received certification of that IRB approval.

TO: FDA/Document Mail Center

FROM: DFG/Symbion

DATE: December 5, 1985

RE: IDE Supplement - **Bridge to Transplant IDE #G850204**
Supplement to add University of Utah, Dr. William A. Gay

Exhibit I	IRB Approval letter.
Exhibit II	IRB members and affiliations.
Exhibit III	Letter from IRB re TAH program.
Exhibit IV	Members of clinical team, their training and responsibilities.
Exhibit V	Patient consent form.

TO: DFG/Symbion

FROM: FDA/Kshitij **Mohan**

DATE: December 6, 1985

RE: **"BRIDGE TO TRANSPLANT" IDE #G850204**
Nonapproval because of deficiencies in protocol and consent form. (5 pages of additional questions)
Denial of "umbrella Policy" on all studies of TAH and VAD's.
Nonapproval of St. Lukes Medical Center in Phoenix and Milwaukee (Vaughn and Tector) until all deficiencies stated in nonapproval of Bridge to Transplant IDE supplement have been satisfactorily addressed.

TO: FDA/William G. Letzing

FROM: DFG/Symbion

DATE: December 9, 1985

RE: **"Bridge to Transplant" IDE # G850204**

Patient report on Michael Drummond from Dr. Jack Copeland, University of Arizona, Tucson, Arizona.

TO: FDA/Abhijit Acharya

FROM: Howard Holstein/Symbion counsel

DATE: December 16, 1985

RE: Potential FDA statements to the public following the December 20th panel recommendations.

TO: FDA/Dockets Management Branch

FROM: R. Jarvik/Symbion

DATE: December 23, 1985

RE: GUIDANCE FOR THE EMERGENCY USE OF UNAPPROVED MEDICAL DEVICES

TO: DFG/Symbion

FROM: FDA/Kshitij Mohan

DATE: December 31, 1985

RE: **"Bridge to Transplant" IDE G850204**

Follow up to FDA's letter of December 6, 1985. Notification that previous approved centers (Abbott-Northwestern, University of Pittsburgh and University of Arizona) will be subject to all requirements of new IDE if approved. Documentation must be submitted within 60 days from approval of IDE G850204.

TO: DFG/Symbion

FROM: FDA/Kshitij Mohan

DATE: December 31, 1985

RE: **JARVIK-7 total arificial heart - 70cc**
Report from Dr. Lyle Joyce, Abbott Northwestern, 70cc Emergency Use Option - exercised.

TO: R. Jarvik/Symbion

FROM: FDA/Kshitij Mohan

DATE: December 31, 1985

RE: CIRCULATORY SYSTEM DEVICES PANEL
Recommendations made to FDA regarding further permanent implantations of the TAH. Request for additional information, revised protocol, etc., within three weeks.

TO: FDA/Document Mail Center

FROM: DFG/Symbion

DATE: January 14th

RE: Total Artificial Heart - IDE #G810057
Revisions to protocol and response to specific questions raised in FDA's December 31st letter and panel's questions.

(Desk copy sent to William Letzing)

TO: FDA/Kshitij Mohan

FROM: DFG/Symbion

DATE: January 9, 1986

RE: Correspondence **JARVIK-7 total artificial heart - 70cc**
Response to letter of December 31, 1985 concerning the use of the J-7-70cc acknowledging request for data and report from Dr. Lyle Joyce. Abbott Northwestern.

TO: FDA/Kshitij Mohan

FROM: DFG/Symbion

DATE: January 15, 1986

RE: **JARVIK-7® total artificial heart - 70cc**

Synopsis report on use of J-7-70cc by Dr. Lyle Joyce at Abbott Northwestern. "Preliminary Clinical Report of the Implantation of the Mini JARVIK-7 in Mary Lund."

Mr. VOLKMER. Thank you very much, Doctor Jarvik.

I will now proceed with Dr. Wolfe.

Dr. WOLFE. Chairman Volkmer, and members of the subcommittee, thank you very much for holding the hearings.

In the last 10 years since the medical device amendments passed there have been far too few such hearings overseeing what has happened in this first decade of regulation by the Federal Government of medical devices, following at great distance the earlier regulation of drugs, and foods and other FDA regulated items.

Before going into the answers to specific questions that you put forth, I would just like to make a couple of general comments, and agree with at least a couple of things that Dr. Jarvik has said, because on other things I think we disagree.

There is no question the American public wants success, whether it is in a space program, or in something that can improve the quality of life. There is also no question that somewhere in the long run, the quality of life for tens of thousands of Americans who have heart disease, or who might otherwise get heart disease, will be improved.

I think that it is more likely because it is going to come through prevention in the long run, than through treatment. It is certainly possible and has been stated now for 20 years that at some point in time an artificial heart will be developed that will be implanted yearly in that many people.

The notion, even back then, before transplants really became done very much, was that it would be far easier to address the problem which is tens of thousands of people who are severely enough ill to need some kind of intervention. It is easier to address it with something that you can reproduce, at will, than with a transplant.

Unfortunately, in, now, 20 years, we have gotten slightly closer to it but I think it is still a long way off.

The last thing that Dr. Jarvik said, that I agree with, was the description of recipients who made the difficult decision along with their families to have the artificial hearts implanted, and used the phrase that they made the decision to enter the unknown. There is no question that it is true, A; and B, up to a point it has to be unknown if it hasn't been done before.

But C, now several years later it isn't quite as unknown as, perhaps, it was then. There have been some unfortunate consequences in the people who had permanent implants.

And I guess the whole question of what is known and what is unknown, in terms of the informed consent issue, and in terms of FDA's role, is something that I worry a lot about.

The first thing he said that I disagree with—and then I will go into the answers—the question is that the artificial heart program need not have as much attention from FDA. If anything, it needs more attention; and I will go into some specific examples of that.

The questions that I was asked to respond to were, first, scientific considerations used for approval of the Jarvik-7 and other artificial hearts. To fully answer this question would require accessed information and data, which, as will be discussed in answer to another question, are believed to be proprietary, trade secret; which are, therefore, kept secret from the public and most of the scientific community.

HEW or now HHS reports for 1969, 1973, 1978, 1985, have repeatedly identified the incompatibility between human and animal blood and the synthetic materials from which the heart are made as the major unsolved problem leading to abnormally increased blood clotting and strokes, or conversely, to excessive bleeding in efforts to diminish the increased blood clotting; damage to red blood cells; immunological problems; infections; and other complications.

I briefly want to review because, I guess, I am a firm believer in history, and I also have the conflict of interest of having been at NIH and believing in at least the bulk of what NIH does, particularly in current direction in these areas.

In 1969, I would just like to briefly quote from a report called, "Cardiac Replacement: Medical, Ethical, Psychological and Economic Implications"; a report by the ad hoc task force on cardiac replacement, National Heart Institute, as it was then called:

> The most serious technical problem that confronts the artificial heart program is the development of a material which is entirely compatible with blood. To varying degrees all materials examined to date have tended to damage red blood cells and other formed elements of blood; to promote clotting and to generate abnormal plasma proteins. The abnormalities in the proteins range from denaturation, to subtle, but important changes in their immunogenic properties.
>
> In contrast, the ideal material must not only produce none of these harmful effects, but it must also meet an imposing array of additional specifications. It should not modify blood or tissue electrolyte composition; not cause allergic or toxic reactions, not interfere with the body's normal defense mechanisms; not cause or promote the developmenmt of cancer; nor otherwise harm the blood or tissue.

It went on to say:

> In contrast to the use of synthetic linings, is the prospect of developing a nearly natural biological lining. For this purpose, embryonal cells have been grown on a framework to provide a pseudo-intima.
>
> This biological lining affords the prospect of producing a compatible interface between blood and the prosthetic device.

Now I will mention later an exciting report on this topic in last week's issue of Science Magazine.

Continue:

> At the time of this report, the prospects are bright but trials are as yet insufficient.

This is 1969.

In 1973, another report called "The Totally Implantable Artificial Heart: A Report of the Artificial Heart Assessment Panel of the National Heart and Lung Institute," as its name was then extended; called:

> The basic problems have beset the development of circulatory assist devices despite remarkable improvements in design and performance. Prosthetic materials used as pump linings have been consistently harmful to blood.

The report went on to state that before clinical application, the artificial heart should:

> Create no physiologically unacceptable deleterious effects to blood and tissues, should be constructed of materials that do not damage the cellular and molecular elements of the blood.

It went on to say:

> Many new materials are currently under investigation. Most promising of these is a pump lining composed of living, self-regenerating intima; intima being the normal lining of a blood vessel.
>
> However, at present, there is still no synthetic lining that can reliably be used as a basis for a totally implantable artificial heart.

That is 1973.

Moving on to 1978, by the then National Heart, Lung, and Blood Institute; longer name:

> The scientific knowledge accumulated in the last 10 years in the area of blood-material interaction has hardly begun to be coherently organized in a predictive science. Currently, a major roadblock to the development of materials to handle and process blood is the lack of an operational definition of blood compatibility.

And moving on to last year's report, from the Heart Institute, National Heart, Lung, and Blood Institute: "Present and Future of Cardiac Assist Devices," a report summarized by Dr. Watson:

> A need still persists to develop a unifying hypothesis in the basic mechanisms of blood/material interactions and reliable short-term methods for evaluating the potential long-term clinical consequences of an implanted device.

Given the continuing—and now going to my own remarks—the summaries of these earlier reports, including one last year, given the continuing failure to solve these serious problems, why was permanent human implantation allowed in the first place?

The second question I was asked to respond to was, the cost versus benefit to society of artificial heart implants.

In discussing the benefit to society, the issue of a totally implantable heart including the power source, obviously, versus the tethered-to-a-large-engine version—the dichotomy to these two versions arises. NIH appears to have rejected the latter alternative and is placing the emphasis of its research funding on a totally implantable device with human trials not expected until 1994 according to a recent report from NIH.

At least two messages from this new NIH priority are clear. And it is a new priority because, as Dr. Jarvik mentioned, he wishes there were more funding for the pneumatic approach, and certainly in the past there was. NIH provided something like $10 million over a number of years to Utah to do important research leading to some of the work that is going on now in other work, and that research funding for those approaches is diminished.

The two messages, at least two messages from this new NIH priority are clear.

First, the benefit to society is always of a magnitude greater if individuals are not tied to an external engine with the obvious detriment to their quality of life, than if they have one totally implantable.

Second, the 1994 date for the first human implantation of a totally artificial heart, I believe, is much more realistic. But perhaps now, 20 years after it, they said around the corner; perhaps that isn't realistic. But I assume that it is at least more realistic considering the present lack of progress toward solving the blood/material incompatibility problems which now plague the artificial heart program.

Now, I am not saying there has been no progress at all. Obviously, even the sequence of messages I wrote—I read, there have been some problems—there has been some progress, but there are significant problems as witnessed by the strokes that have occurred in people with these hearts implanted.

Exciting progress was reported last week in Science Magazine, January 24th issue, in which an artificial blood vessel, made of collagen, dacron, and natural constituents, was lined with endothelial cells—the natural lining of blood vessels—and functions physiologically in terms of production of anticlotting factors, such as prostacyclin.

The broader issue in terms of the cost versus benefit-to-society equation is, what we can do now, and in the 25 years down the line from now, in the year 2010. For example, the line of people with severe heart disease awaiting either a transplant, or, if it is ever developed the widespread clinical application of a totally implantable heart. This line is short, is as short as possible.

And here again I agree with Dr. Jarvik fully; more education of the public and long overdue education of physicians and other health care professionals about the role of diet and evolution of heart disease, as well as much more aggressive efforts toward much less smoking are sorely needed. We attack the proposal made last month by AMA, intended to discourage participation in litigation against the cigarette companies.

They eventually changed their proposal on that basis, and anything including massive law suits, hopefully successful, against the cigarette industry has to be done, including changes in advertising to stop this blight.

The third and fourth questions, I am combining. They are, three, the selection of patients for artificial heart implants; and four, bridge-to-transplant use versus permanent use of artificial hearts at the present state of our knowledge

These two questions must now be considered together since the question of patient selection is a different one depending on which of these two uses are being contemplated. The long-term goals of all this research are, of course, if possible, to develop a device that can be used in large numbers of people.

The short-term goals really have to be: First, what is best for the patient; second, will some advance in the understanding of the whole question of artificial hearts be derived from implanting yet another device in the patient.

First, the permanent issue. FDA, in my view, has unfortunately refused to stop further permanent implants now despite the tragic and unexpected results in the first five people in whom the Jarvik heart was implanted.

However, the so-called forces on the marketplace, aided, I suspect, by modifications in both the formal and informal process of informed consent probably thanks to Dr. DeVries, have conspired to cause a *de facto* moratorium on permanent implants for almost 10 months.

An additional, perhaps, causal reason for this change is that the increased availability of transplants is always a considerably better alternative for the patient. I believe, in a sense, there is a double standard here in terms of the very tight surveillance over Dr. DeVries and his work, which, I think, is appropriate, versus what seems to be less than tight surveillance by the FDA over the bridge-to-transplant use.

As long as there is a shortage of natural hearts available for transplant relative to the 10,000 or more people who could benefit significantly from such an operation, the use of an artificial heart as a bridge-to-transplant will inevitably displace a waiting candidate who is a better risk for a transplant, by a person who, in almost every case, is not as good a candidate.

The other important issue here, however, is that even if the concept of temporary implantation is thought to be a valid one, and let's assume for the sake of argument that it is, there are alternatives to the total artificial heart, Jarvik or otherwise.

According to NIH, and I note that Dr. Lenfant discusses this in his testimony, approximately 20 patients awaiting transplant have had a bridge device implanted. We have gotten a figure of 30, I believe, it is 20.

Approximately two-thirds have had a left ventricular assist device in which the natural heart is left in place until transplantation; and about one-third had a total artificial heart such as the Jarvik or Penn State.

Although the results as far as success rate were said to be similar, this data needs to be made public so cardiac surgeons, other physicians and patients and their families will be fully informed about these alternatives.

I note, and I will read just one sentence from it because it will be discussed in greater detail, the longest surviving bridge patient was supported with an implantable electrically powered ventricular assist device. I am concerned that when either the Jarvik heart is put in on an interim basis or the left ventricular assist device is put in, that the decision has more to do with which of these is being done by the person who is putting the device in, than by a thorough public review of which has a better record.

The record of the left ventricular device includes occasions when it was used that are some time ago, and my guess is that more recently the record must be better. I do not know whether, if one looks at longevity, complications, mortality, and everything else, there is a difference between the two.

If there isn't, so be it.

If there is, which one is better?

That certainly is something that needs to be known so that if there are going to be more bridge implants, as a short-term alternative before a natural heart is found, the best possible selection for the patient is made.

The last question, which I was asked to respond to is the quote: "Proprietary information in light of adequate review of artificial heart implants."

The idea that for drugs or for medical devices, such as the artificial heart, important data concerning safety or efficacy should be kept secret from the public, from most of the medical and research community, and even from most of the people engaged in research on similar drugs or devices, is dangerous, as well as, indefensible.

In the present case, it would be important to know the composition of the lining of the artificial heart; Dr. Jarvik mentioned polyurethane bellows but when I made a request for the detailed information on each of the parts of the heart I was told it was proprietary information.

It would also be important to know the original and present versions of the protocol and informed consent sheets and the detailed data on what has happened to each patient as far as infections, immunological disturbances, kidney damage, red blood cell destruction, liver damage, brain damage, and mental status.

All of this information is said to be "proprietary," despite the fact that one of the main competitors of the Jarvik heart, Penn State University, has had one of its biomedical engineers, Dr. David Geselowitz, on the FDA advisory panel. He has been cleared of all conflicts of interest. He was at the beginning of the FDA hearing last month, in January—in December, rather, and he is able to learn all these details.

In summary, I am certainly in favor of progress in the area of relieving the problem of cardiovascular disease. It is possible that ultimately one of the kinds of relief may be an artificial heart.

It is unlikely that the one that is going to be implanted in tens of thousands of people is going to be very similar to the one that is now used basically on a bridge basis.

I have serious questions as to whether or not any of these devices should be implanted permanently. And until there is more public discussion of the relative merits of the several left ventricular assist devices that are available for bridge purposes, and the Jarvik-7 I think that there should be a pause in what is going on there.

I understand the emergency nature of these things; one cannot anticipate emergencies the day before they happen, but looking toward continuing emergencies, they're obviously going to occur. I think there is an obligation on the part of the FDA to make public all the detail comparisons between these two kinds of devices in terms of the bridge use if we are going to continue allowing, or in some cases, not allowing the occurrence going on, nevertheless, of the bridge use of the artificial heart or other assist devices.

Thank you.

[The prepared statement of Dr. Sidney M. Wolfe follows:]

SUMMARY OF REMARKS BY SIDNEY M. WOLFE, M.D.

Public Citizen Health Research Group

HOUSE SCIENCE AND TECHNOLOGY COMMITTEE HEARING ON ARTIFICIAL HEART IMPLANTS

February 5, 1986

Chairman Volkmer and Members of the Subcommittee. Thank you for holding these important hearings, which represent an effort to oversee the ten year old medical device amendments.

1. The scientific considerations used for approval of the Jarvik-7 and other artificial hearts

To fully answer this question would require access to information and data which, as will be discussed in the answer to question 5, are believed to be "proprietary", and which are therefore kept secret from the public and from most of the scientific community. HHS (HEW) reports from 1969, 1973, 1978, and 1985 repeatedly identify the incompatibility between human (or animal) blood and the synthetic materials from which the artificial heart is made as the major unsolved problem leading to abnormally increased blood clotting and strokes, excessive bleeding in efforts to diminish the increased blood clotting, damage to red blood cells, immunological problems and other complications. Some examples:

1969 Cardiac Replacement: Medical, Ethical, Psychological and Economic Implications; A Report by Ad Hoc Task Force on Cardiac Replacement, National Heart Institute.

> The most serious technical problem that confronts the Artificial Heart Program is the development of a material which is entirely compatible with blood. To varying degrees, all materials examined to date have tended to damage red blood cells and other formed elements of blood, to promote clotting and to generate abnormal plasma proteins; the abnormalities in the proteins range from denaturation to subtle, but important, changes in their immunogenic properties. In contrast, the ideal material must not only produce none of these harmful effects, but it must also meet an imposing array of additional specifications. It should not modify blood or tissue electrolyte composition, not cause allergic or toxic reactions; not interfere with the body's normal defense mechanisms; not cause or promote the development of cancer, nor otherwise harm the blood or tissue. . . .
>
> In contrast to the use of synthetic linings, is the prospect of developing a nearly natural biological lining. For this purpose, embryonal cells have been

> grown on a framework to provide a pseudo-intima. This biological lining affords the prospect of producing a compatible interface between blood and the prosthetic device. At the time of this report, the prospects are bright but trials are as yet insufficient.

1973 The Totally Implantable Artificial Heart: A Report of the Artificial Heart Assessment Panel of the National Heart and Lung Institute.

> Some basic problems have beset the development of circulatory assist devices despite remarkable improvements in design and performance. Prosthetic materials used as pump linings have been consistently harmful to blood. . . . (page 18)

The report went on to state that before clinical application, the artificial heart should:

> create no physiologically unacceptable deleterious effects to blood and tissues, . . . should be constructed of materials that do not damage the cellular and molecular elements of the blood . . . . (page 35)

> Many new materials are currently under investigation. Most promising of these is a pump lining composed of living, self-regenerating intima -- However, at present, there is still no synthetic lining that can reliably be used as a basis for a totally implantable artificial heart. (page 37)

1978 Report of the Task Force on Biomaterials to the Cardiology Advisory Committee of the NHLBI, reprinted in Artificial Organs, 1978, Vol. 2, No. 2.

> The scientific knowledge accumulated in the last ten years in the area of blood-material interaction has hardly begun to be coherently organized in a predictive science. . . . Currently, a major roadblock to the development of materials to handle and process blood is the lack of an operational definition of blood compatibility.

1985 Present and Future of Cardiac Assist Devices, John T. Watson, N.H.L.B.I. in Artificial Organs, 9(2): 138-143, 1985.

> [A] need still persists to develop a unifying hypothesis in the basic mechanisms of blood/material interactions and reliable short-term methods for

evaluating the potential long-term clinical consequences of an implanted device.

Given the continuing failure to solve these serious problems, why was permanent human implantation allowed in the first place?

2. Cost vs. benefit to society of artificial heart implants

In discussing the benefit to society, the issue of a totally-implantable vs. the tethered-to-a-large-engine dichotomy arises. NIH appears to have rejected the latter alternative and is placing the emphasis of its research funding on a totally-implantable device with human trials not expected until 1994. At least two messages from this new NIH priority are clear: first, the benefit to society is orders of magnitude greater if individuals are not tied to an external engine with the obvious detriment to their quality of life; second, the 1994 date for first human implantation of a totally implantable artificial heart is much more realistic considering the present lack of progress toward solving the blood/material incompatibility problems which now plague the artificial heart program. Exciting progress was reported last week in Science magazine (Vol. 231, pp. 397-8, Jan. 24, 1986) in which an artificial blood vessel, made of collagen, dacron, and natural constituents, was lined with endothelial cells (the natural lining of blood vessels) and function physiologically in terms of production of anti-clotting factors such as prostacyclin. The broader issue as far as the societal cost/benefit equation is what can we do now so that 25 years down the line - in 2010, the line of people with severe heart disease awaiting either a transplant or, if it is ever developed for widespread clinical application, a totally-implantable artificial heart is as short as possible? More education of the public and long-overdue education of physicians and other health care professionals about the role of diet in the evolution of heart disease as well as much more aggressive efforts toward much less smoking are sorely needed.

3. Selection of patients for artificial heart implants

4. Bridge-to transplant use vs. permanent use of artificial hearts at the present state of our knowledge

These two questions must now be considered together since the question of patient selection is a different one depending on which of these two uses is being contemplated.

Permanent Implant: FDA has unfortunately refused to stop further permanent implants now despite the tragic and unacceptable results on the first five people in whom the Jarvik Heart was implanted. However, the so-called forces of the marketplace, aided, I suspect, by modifications in both the formal and informal process of informed consent probably thanks to Dr. De Vries, have conspired to cause a de facto moratorium on permanent implants for almost ten months. An additional or, perhaps, causal reason for this change is the increased availability of transplants, always a considerably better alternative for the patient.

Bridge-to-Transplant Use: As long as there is a shortage of natural hearts available for transplant relative to the ten or more thousand people who could benefit significantly from such an operation, the use of an artificial heart as a bridge-to-transplant will inevitably displace a waiting candidate who is a better risk patient for a transplant by a person who, in almost every case, is not as good a candidate. The other important issue here, however, is that even if the concept of temporary implantation is thought to be a valid one, there are alternatives to the total artificial heart, Jarvik or otherwise. According to NIH scientists, approximately 30 patients, awaiting transplants, have had a bridge device implanted. Approximately two-thirds had a left ventricular assist device (LVAD) in which the natural heart is left in place until transplantation and about one-third had a total artificial heart such as the Jarvik or Penn State. Although the results, as far as "success" rate were said to be similar, this data needs to be made public so cardiac surgeons, other physicians and patients and their families will be fully informed about these alternatives.

5. "Proprietary" Information in light of adequate review of artificial heart implants

The idea that for drugs or for medical devices such as the artificial heart, important data concerning safety or efficacy should be kept secret from the public, from most of the medical and research community and even from most of the people engaged in research on similar drugs or devices is dangerous as well as indefensible. In the present case, it would be important to know the composition of the lining of the artificial heart, the original and present versions of the protocol and informed consent sheets and the detailed data on what has happened to each patient as far as infections, immunological disturbances, kidney damage, red blood cell destruction, liver damage, brain damage and mental status. All of this information is said to be "proprietary", despite the fact that one of the main competitors, Penn State University, has one of its biomedical engineers, Dr. David Geselowitz, on the FDA Advisory Panel. He has been cleared of all conflict of interest and able to learn of all these details.

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Curriculum Vitae

Sidney M. Wolfe, M.D.

B.S., Chemistry, Western Reserve University, Cleveland, Ohio	1960
M.D., Western Reserve University, Cleveland, Ohio.	1965
Intern (Internal Med.), Cleveland Metropolitan General Hospital, Cleveland, Ohio.	1965-66
Clinical Associate, Section on Physiology and Clinical Nutrition, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland	1966-69
Resident (Internal Med.), Cleveland Metropolitan General Hospital	1969-70
Senior Staff Fellow, Section on Physiology and Clinical Nutrition, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland.	1970-72
Director, Public Citizen Health Research Group, Washington, DC	1972- Present
Consultant, N.I.H., Bethesda, Maryland, Member, Carcinogenesis Clearinghouse, National Cancer Institute	1976-78
Member, Joint Coordinating Council for Project Sleep: The National Program on Insomnia and Sleep Disorders	1979- Present
President, Public Citizen, Inc., Washington, DC	1980-82
Visiting Professor, Cornell University, Hospital Administration Program. Ithaca, N.Y.	1982- Present
Consultant, National Cancer Institute, DES Task Force Bethesda, Maryland	1985

Areas of Clinical Research

1) Clinical and physiological studies of etiology and treatment of alcohol withdrawal syndrome.

2) Laboratory studies of mechanism of secretion of mammalian cells; platelet metabolism and cellular mechanisms of blood clotting.

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Public Citizen Health Research Group Activities

Public Citizen is a non-profit citizen research, lobbying and litigation organization founded in 1971 by Ralph Nader. The Health Research Group, one of five affiliated arms of Public Citizen, fights for protection against unsafe drugs, foods, medical devices and workplaces, and for greater consumer control over health decisions.

HEALTH RESEARCH GROUP BOOKS

1. Kaufman, J., Rabinowitz-Dagi, L., Levin, J., McCarthy, P., Wolfe, S. and Bargmann, E., *Over the Counter Pills That Don't Work*, Public Citizen Health Research Group, 1983.

2. Bargmann, E., Wolfe, S. and Levin J., *Stopping Valium and Ativan, Centrax, Dalmane, Librium, Paxipam, Restoril, Serax, Tranxene Xanax*, Public Citizen Health Research Group, 1982.

3. Wolfe, S., Coley C. and the Health Research Group, *Pills That Don't Work: A Consumers' and Doctors' Guide to 610 Prescription Drugs that Lack Evidence of Effectiveness*, Public Citizen Health Research Group, 1981.

4. Warner, R., Wolfe, S. and Rich, R., *Off Diabetes Pills: A Diabetic's Guide to a Longer Life*, Public Citizen Health Research Group, November 1978.

5. Nash, G. and Wolfe, S., *Taking the Pain out of Finding a Good Dentist*, Public Citizen Health Research Group, 1975.

ADDITIONAL FOLLOW-UP QUESTIONS FOR THE RECORD [*]

APRIL 7, 1986.

Dr. SIDNEY M. WOLFE, M.D.,
Director, Public Citizen Health Research Group,
Washington, DC.

DEAR DR. WOLFE: Enclosed is a copy of the transcript from the February 5, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight about artificial hearts. Attached to the transcript are instructions for submitting requests for changes or clarifications. Please review these instructions and the enclosed transcript of your remarks carefully.

The Subcommittee would also appreciate your written responses to the following questions:

1. In your view, are FDA's guidelines for emergency artificial heart implants adequate?
2. If not, how could they be improved?

Your copy of the transcript, together with any written requests for changes and your responses to the above questions, should be returned by April 24, 1986 to: Dr. Irene Glowinski, Subcommittee on Investigations and Oversight, 822 House Annex I, Washington, DC 20515-6307.

Your testimony at the hearing was extremely valuable to the Members, and I want to extend our thanks for your participation and service to the Subcommittee.

Sincerely,

HAROLD L. VOLKMER, *Chairman,*
Subcommittee on Investigations and Oversight.

Mr. VOLKMER. Thank you very much, Dr. Wolfe.

We will now turn to questioning, and I will first recognize the gentleman from California for any questions he may have either of Dr. Jarvik or Dr. Wolfe.

Mr. PACKARD. Thank you very much, Mr. Chairman.

I sincerely appreciate the testimony of the witnesses this morning. I think they were very professionally given and very well thought through.

This is a very fascinating and interesting field, and certainly we are in the beginning stages of research and development in this area, and I think that is obvious, and obviously that is the reason for these hearings, and for the interest, not only for this committee, but I am sure the American people and the medical profession.

Let me get to some questions I have of you, Dr. Wolfe, inasmuch as your testimony is the most recent.

The —do I understand your testimony to mean that you would suggest a placing on hold of any further implant procedures of artificial devices in order to wait until there is further information in terms of the concerns that you expressed?

Dr. WOLFE. Two answers. In terms of permanent implantation, I would certainly agree that there should be a hold. I think FDA should have done that themselves. De facto, it has occurred. It has been 10 months since the Jarvik heart has been put in.

As far as the second part of the question, which is on the bridge use, I think it would not take very long, a couple of days, to collect all the data on these, I guess. 21 patients who have had some kind of mechanical device put in as a bridge-to-transplant, and see which one, if such is the case, is better.

There are a number of groups in the country who have looked on these, both in the animal stage, and a smaller number of groups who have been engaged in putting these into humans.

---

[*] No response from Dr. Wolfe to this letter as of June 19, 1986.

I guess my plea is if we are going to be able to give informed consent to the patients, let's assume on emergency basis, need one of these, why not make available to them the best one. I think that as I mentioned before, if you happen to be in a city where the person is putting in the Jarvik as the bridge device, it is possible the same investigator has had experience with the left ventricular device; but which one is better?

If you happen to be living in a city where there is experience with the left ventricular assist device, it is possible that the Jarvik heart is better. I don't know the answer to those questions.

I was told that the success-rate quote, quote, is equal but I don't take into consideration mortality, complications, quality of life, and other things.

And as I said, I noted the comment that Dr. Lenfant will make in his testimony is that the longest surviving patient happened to have the left ventricular assist device. So I guess, what I am saying in very short order, we could analyze the data on every human who has had one of these put in on a bridge basis and make more public the basis for deciding which is better.

If one is clearly better than the other, then I think the one that isn't doing as well, should not be allowed on a bridge basis. And the other one should be encouraged to go on.

As I say, it is possible that they are exactly the same. I just don't know the answer to these questions because that data is kept secret. It should not be a secret.

All that should be analyzed carefully by the people who are charged with this responsibility and that will make a much better future for the bridge issue.

Again, I mention, I think there is a double standard, Dr. DeVries is clearly being regulated much more thoroughly and carefully than the people who are at least putting in the Jarvik device on an interim basis. I don't know whether the amount of regulation for people who are putting in left ventricular device what that amounts to, I—it's all kept secret.

Mr. PACKARD. It would appear to me if we followed that procedure that we would limit our research and our development into only one direction. Looking only at one device that has been perceived by somebody, either FDA or NIH, or whoever, or physicians themselves, that this device is better.

My own experience has been that physicians and professional people will have different attitudes on different procedures and different equipment.

And some will use one set of equipment because of their own personal preferences and experiences. And others will use an entirely different set that may not—that may fit into their hands much better.

Are you suggesting that we narrow then this whole field in one direction only?

Or do you feel that there is possibility of a variety of experimentation being done, and some successfully, well, their success being different at different times in each of those areas?

Dr. WOLFE. I like to separate out for the sake of answering your question, preclinical research, which includes the engineering and the implantation in the studying the devices in vitro, and the implantation in animals from the clinical application.

Really, all I am saying is that as much as research is appropriate, given our resources and given, I think, the lack of adequate input into prevention, as much research should be done as is appropriate.

But again, if one looks again at the timeline developed by the National Heart Institute, the National Heart, Lung, and Blood Institute—I give away my age in calling it what it used to be called—they have a timeline where they are in the process of letting out some contracts ultimately to develop a totally implantable heart.

They are talking 8 years between now and the time when it may be implanted in humans.

That kind of research, I think, is appropriate to do. I have no qualms with that, I am simply talking about whether after doing one or two or three or four different kinds of research which are going on, and will continue to go on, you will find one is better than the other; and that is the one that you say, let's go forth and do some human trials on.

I think if there is a big difference between two different avenues of research as they evolve in the laboratory, or from early clinical experience, the one that is better should be pursued, or allowed to continue, in terms of human implants.

So, I am really separating out just human experimentation human implantation from the longer process, often, of the development, the engineering development, and the animal experimentation.

Mr. **Packard**. You made the statement in your testimony, Dr. Wolfe, that what is best for the patient is of paramount importance.

Who should determine that; who should determine which device is implanted; and who should determine whether a device or a treatment should be prescribed?

In your judgment, should that be done by an agency such as FDA, or other agencies; should that be done by—through the doctor/patient relationship?

What generally, would you suggest as being the procedure to determine what is best for the patient?

Dr. **Wolfe**. Well, I'd like to reflect back on a statement that Dr. Jarvik made. He defined acceptable risk as the situation whereas the person who is at risk understands the risk and accepts it.

That is certainly one element of it once it has gotten past some other hurdles.

I'd like to quote from the FDA's own definition of what the criteria should be for approving an artificial heart for implantation, which is the first phase of informed consent, that Dr. Jarvik described.

First, where the risks to the subjects are outweighed by the anticipated benefits to the subject.

Second, to evaluate the importance of knowledge to be gained, whether the study is scientifically sound.

Now, at the individual, personal level, if the FDA has decided to allow the implant to go on, the FDA has obviously decided that for that individual, the potential individuals that fit into that category, that that implantation, artificial heart, or otherwise, is better than the alternatives.

What are the other alternatives?

Well, in the case of permanent implantation, one of the reasons why there haven't been permanent implants for this period of time is that the alternatives now include more for people than 1 year, or 2, or 3 ago, a transplant.

So, that if a person is in a situation that has Class-4 cardiac disease, really disabled, and something needs to be done; if the best alternative is a transplant, that person has to be informed of that; if they are informed of it they are not likely to pick an alternative that isn't so good.

So, it is a combination of the Federal Government in its careful consideration as to whether to allow human experimentation of any kind to go on, and having done that, a carefully drawn out, understandable, up-to-date informed consent sheet.

The informed consent sheet for the artificial heart today has to be different than it was, different than it was 3 to 4 years ago. I have no doubt that it is.

The fact that I can't find that out is annoying. But I have faith in Dr. Jarvik, Dr. DeVries, FDA, and everyone else that it is a different informed consent sheet. That that is one of the reasons why permanent implants haven't been done.

So, it is really a combination of a Federal role, and the concept of informed consent. In between those two levels are things such as institutional review boards at the institution where the operation is done that need to provide some kind of oversight.

It is a complicated process. It is something that really is a creation of the last 10 or 20 years, not just with artificial devices such as the artificial heart, but a lot of other things.

We are learning. I think it is getting better than it used to be. But it is a difficult kind of process; but the Government has to be involved.

The idea as expressed during the legislative hearings in 1974 and 1975, when the medical device amendment was being considered, that surgeons' creativity shouldn't be stifled by Government having laws such as this, which was expressed by a number of surgeons testifying. I disagree strongly with that.

I am all in favor of the creativity of artists, surgeons, or anyone else, but it needs to be checked by some proper Government surveillance; it is a difficult balance to figure out what the proper Government surveillance is, and what is good surveillance today may be thought inadequate surveillance tomorrow.

I hope I have not avoided your question, it is a difficult one I tried to answer.

Mr. PACKARD. Yes; thank you very much.

Dr. Jarvik, you have referred in your testimony to the high quality of life that you are seeking in the use of artificial devices as implants.

What would you consider, if you were to define a high quality of life, how would you define it in terms of post-heart implant devices?

Dr. JARVIK. Well, I think it can be well defined by considering what you would consider as a normal life.

What we mean is that a patient is free of pain; that they feel strong; that they are able to be mobile in society; that they get up and walk around; and they can conduct all normal activities. We think that is a high quality of life.

There are many circumstances in which life of far less quality is obtained, not only with artificial heart, but in many disease conditions, where we certainly stick by our people and do everything we can for them.

But what we mean is true mobility, true normalcy, and the nuisance value of having to change the batteries in your vest, or the package that you carry, we think, diminishes it a little bit. But really the people that have severe heart disease, can barely breathe, they suffer pain, they can't get out of bed and walk across the room without feeling weak. We are talking about people being generally normal.

Mr. **Packard**. With all of the devices now in existence around the world that are being used for experimentation, do you see at this point any device that clearly outpaces the other in terms of concept, and in terms of performance, that provides a higher quality of life than others?

Again, in terms, again, experience?

Dr. **Jarvik**. I think that—there is a concept that should be introduced, that—that NIH for many years has basically supported. And that is the idea that what is needed is a family of devices.

The clinical conditions of patients with heart disease cannot be treated with one device only. It is definitely clear that in some circumstances that a temporary left-heart assist device can allow a dismally sick natural heart to recover sufficiently for the patient to become a long survivor with good restoration of heart function.

That is known for sure. There are cases in which it is unclear that a patient's heart can recover, in which it is appropriate and ethical to put in a temporary left-heart assist device hoping to have that heart recover. If they cannot and they are unable to be supported, then you can go on to a more extreme measure such as heart transplant.

There are cases in which a total artificial heart may be needed as a bridge and cases in which both right-heart assist and left-heart assist together may be a better choice for a bridge.

And these decisions, in terms of clinical conditions, in some cases are quite clear. And in others, they are unclear, because we do not have enough information to know exactly which device is the best to apply.

Symbion is developing a family of devices also. And on the table we have a temporary left-heart assist device together with the total artificial heart.

We intend to develop the permanent implantable left-heart assist device also, now, because I strongly agree with the NIH position.

And I also agree—talking about Dr. Wolfe's comment, that it may be a matter of luck which device is used; at which medical center a particular device is used, and that is true. I think that it would be well if many centers could have available a variety of devices so that in appropriate indications they could select either a heart-assist, either a temporary, or permanent, or a total heart.

That is what we are trying to do. We are trying to provide that.

And just one further comment on the whole thing. I agree with you very much, Mr. Packard, that we should not conclude too early on the basis of a preliminary review of the results of a number of different experimental systems, which is best.

We should encourage the development of all of them. And there is no doubt in my mind that the need for patient care is so broad, and the opportunity to learn is so great, that we could well use another 10 artificial heart systems in this country that were very broadly examined.

We would speed progress, and we would learn a whole lot more, and a lot of people would be helped.

Mr. **Packard**. I won't take much more time; I realize there are others who want to ask questions.

In your testimony, Dr. Jarvik, and also in Dr. Wolfe's comments, he alluded to the fact that deficiencies in the material itself, that is used, is in some cases incompatible with human blood, and has maybe been some of the reasons for stroke and problems, complications that have resulted.

Do you—have you had the opportunity to evaluate the condition plus also the longevity of the material itself. You are talking about 2 years now, the device lasting up to 2 years, and with the hope to 5 or even 7, or 8 years in the future. Again, simply looking at the material itself, have you been able to evaluate on those unsuccessful cases?

Now, I shouldn't use the word unsuccessful; I mean those who have passed away.

Have you been able to evaluate the heart—the device, I should say, in terms of its deterioration during that period of time that it was being used and in terms of its integrity, its life expectancy of the material itself.

Dr. **Jarvik**. Yes——

Mr. **Packard** [continuing]. To correct the problems that have been alluded to?

Dr. **Jarvik**. Let me first say that I disagree with the concept that we do not have a good biomaterial.

I think that the concept of using a biologic lining is a nice concept, but it's difficult. There have been many studies on that. We worked on that early, and other people are pursuing that now. That is one approach.

Our approach is to use a smooth surface without a biologic lining, meaning no cellular lining on the surface of the heart itself; just blood protein against that surface. And, we feel that is very successful.

In all of the human cases, we have very clean interior to the hearts that we have seen, and the only problem areas have been around the mechanical crevices around the valves and connectors, or where there is some junction in the heart that leaves a seam, a crevice.

The heart is fundamentally free of seams, other than around the valves. We have reevaluated new designs, as I mentioned, and I believe that with existing biomaterials you cannot separate the issue of the design features of the device including the flow pattern; how well it's washed; whether you have a stagnation area where clots can form; and the material itself. You can't separate those.

So, a material if used in a good design will work. You cannot eliminate the question of mechanical durability.

The material that we use now, which is called biomer, which is one of a family of polyurethanes, lasts 4 to 5 years, usually; more than 5 years presently with our existing designs, in terms of flex life.

It is very resistant to creep; it has very good blood compatibilty; it is nontoxic and noncarcinogenic; it is an excellent material.

And I believe with presently available materials with proper design, and no new, fundamental new breakthroughs in materials technology, we can make devices that will remain clean of thrombus and be highly reliable for 8 to 10 years.

Mr. **Packard**. Will that equipment, if there is equipment failure be just as sudden and traumatic as a heart failure in a normal patient?

Dr. **Jarvik**. It depends on the type of failure. We have in the past, you know, our diaphragm has four layers, each layer is about six to seven-thousandths of an inch thick; thickness of a few sheets of paper; and there is a powdered graphite in between the layers so that as they flex they slide in relation to one another.

And coincidentally this technology was evolved in the space program for something called, cryogenic expulsion blatters, where a liquid fuel member at very cold temperatures in space needed to flex a few cycles; By making very, very thin layers they were able to achieve flex cycles of like 30 cycles, with a—with a very thin mylar film.

And it is the same principle, as you make thin layers you reduce the stress. But also you achieve redundancy.

So, if one layer breaks you have a noncatastrophic failure. You can identify that through the noninvasive monitoring of the artificial heart through the computer monitoring system used. And you have time to intervene.

If you have a different type of failure, such as a valve fracture, that can be catastrophic and sudden. In the one case where that happened in Barney Clark. Fortunately, we were able to stabilize his condition by the way we controlled the heart driver and replaced the heart.

So, some failures may be catastrophic, and some may give early warning.

Mr. **Packard**. History has shown thus far that there have been stroke problems as a postoperative complication. And there has been in some cases renal, kidney problems.

What progress has been made and what do you feel are the causes of those kinds of problems?

Dr. **Jarvik**. Well, the bridge-to-transplant application has helped us learn about that, because in Michael Drummond, there was a minor stroke that cleared up completely. But he received a human heart 3 or 4 days after that event and we were able to examine that heart. We had excellent data on anticoagulation parameters.

And we recognized some things which were previously unknown as he rapidly improved. With good hemodynamic function from the artificial heart his liver function returned toward normal; his kidney function became normal; and this rapidly changed the coagulation parameters in his body. The result was that the anticoagulant drugs that were given were of insufficient dose.

So, that was modified. We saw——

Mr. **Packard**. Let me—let me break in there for a moment.

Have your recent implants shown an improvement in these complications, for example, the ones just done this week——

Dr. **Jarvik**. I was coming to that——

Mr. **Packard**. Have you experienced any further complications as far as kidney or stroke problems?

Dr. **Jarvik**. The case of Mary Lund, for example, where the heart pumped 6 weeks. Based on discussions with the Tuscon group, the group in Minneapolis was careful about anticoagulation, and used Heparin anticoagulation. The heart was virtually clean of thrombus. There was a minimal amount of fibrin; very, very minimal in the areas of the crevices of the valves, exactly where we expected there would be a little tiny bit.

There was no stroke, there were no neurological complications. Renal function has been good in the patients who have been transplanted over the last few days. Some of the problems reported that Dr. DeVries had with kidney function, we believe, are related to the way in which the heart driver was set, and that has been greatly improved.

The fact that Mary Lund had complete kidney failure is very interesting because she had complete kidney shut down 2 days before the implant. And with the artificial heart, in about 3 weeks her kidney function returned to normal, and then she was transplanted.

So, now we do feel that we have made a great deal of progress, and understand these issues much better. And we have some additional plans, as I mentioned, to further improve the designs.

Mr. **Packard**. Let me refer back to you, Mr. Chairman, and I will have other questions later.

Mr. **Volkmer**. Yes, I would like to——

Dr. Jarvik, for purposes of the record, I notice that you have a regular Jarvik artificial heart at the table, and also a mini-Jarvik. Could you, just for the record, take one of them—either one, it doesn't make any difference. I understand that both components are the same, and for the record explain as briefly as possible the operation and the components thereof?

Dr. **Jarvik**. Certainly.

The heart is composed of two pumping members called ventricles. This is the left and this is the right. And these replace the lower chambers of the heart—the natural ventricles.

Basically, the function is very simple. There is a compressed air line that drives air into it. Inside the heart there is this flexing diaphragm member which separates the air chamber from the blood chamber.

The simplest analogy to function, is if you were to have a tube going to a balloon. Put the balloon in a glass of water and blow up the balloon. That air would force the water out of the glass and obviously the air wouldn't get into the water itself.

The same thing. The air as it is pumped in, forces the blood out of the heart, but in order to get the proper direction of flow and make it pump forward only, we need two valves.

This one is the inflow valve. The blood comes in, fills the heart, the diaphragm moves back. Then as the compressed air is forced into the heart, that pushes the blood out. The inflow valve closes, the outflow valve opens, and the blood is pumped out to the body, or to the lungs, if it is the right ventricle.

The system then requires some surgical connection method. We use suturing rings that are attached surgically to the remnants of the heart after the natural ventricles are removed. These are sewn in and then the heart is snapped into place. So we refer to these connectors as "quick connects."

After you make the suturing, without the big mass of the heart in the way, you can check that there are no leaks, no bleeding, and so forth, and then come and attach on the heart.

The heart needs an external drive system. In this case we have to show you we have a portable drive system, this is the Helm Holtz portable heart driver, developed originally at the Helm Holtz Institute in Achern, West Germany, and now developed by a subsidiary company that Symbion has in Germany.

It contains complete redundancy. We have a primary and a secondary backup piston compressor in this system, each driven by an electric, brushless dc motor. We have microcomputer systems to control it.

We have a 4-hour primary battery and a 12-hour emergency backup battery. The system is set up in such a way that if there is any malfunction in the primary system it will alarm and switch over to back up.

It doubles the weight of the system, essentially, to carry the backup, and the system weighs about 13 pounds now with emergency batteries.

But we have felt that the highest reliability is important and that it is worth it for the patient to carry that redundancy. And one further thing, if I have a moment. The philosophy of equipment development that we have taken has been an evolutionary philosophy.

This portable system was not available at the time of Barney Clark. There was a nonredundant system which wasn't used but there was a large external drive cart, as you know, which we still use in the bridge-to-transplant patients, and which is primarily used in the two living long-term patients, now.

We feel that as we learn more about this, gain reliability data, we use only the small system. And as we gain human data on the implanted blood pump, we are working on a further system together with NIH, called the electrohydraulic heart, which is a miniature electric motor energy converter, that is about the size of a flashlight battery, a D cell flashlight battery.

It attaches onto the heart, and it provides hydraulic fluid that pumps first from one side of the heart to the other. So, that with what is learned about the blood pumps we will retain that technology, we will retain what we learn about human medical care, patient indications for use, and follow-up care.

And we will use that knowledge, and apply to it further developments that will make it more portable and give us, what we think, is a better, a better ultimate portability and mobility for the patient.

Mr. **Volkmer**. Thank you very much, Dr. Jarvik.

Dr. Wolfe, in listening to your statement and some of your answers to the questions of the gentleman from California, correct me if I am wrong in saying, in general, it appears at least, that if a decision to use the Jarvik heart as a permanent transplant was up to you individually, you, you had that right to make that decision, that your decision would be as of this time, that it would not be used for implantation for a permanent heart transplant; is that correct?

Dr. **Wolfe**. Based on what we have learned for the last 3-plus years since they were put in, my decision would be not to put it in. I think that FDA made a mistake in not reaching the same conclusion in Decmeber when they were asked to decide whether more of the permanent ones should go on.

Mr. **Volkmer**. Now, is that on the basis that the—I know you gave in your statement many of the reasons, but primarily because of the clotting, the attack of the red blood cells, those types of things?

Dr. **Wolfe**. In terms of the permanent implantation, I think the main reason is that—and I think it is the explanation for why, one of the explanations for why there hasn't been one put in for 10 months, even though they are allowed, that the kinds of people, at least most, if not all of the kinds of people who have had a permanent implant put in in the past would be candidates for a transplant.

So, that if you go down to the level of the individual patient, what is best for the patient, what is best since it works better in the long term is a transplant. The reason that the transplant is better is——

Mr. **Volkmer**. Is a human heart——

Dr. **Wolfe** [continuing]. Human transplant, right, because it does not have the kinds of complications, and has a much longer and well-understood record.

Mr. **Volkmer**. Now, are you saying, then, that Barney Clark and the others who have had the permanent transplants were candidates for a human heart transplant?

Dr. **Wolfe**. Well, between the time that Barney Clark was implanted and now, there has been a broadening in the definition of who is suitable as a candidate for a human transplant both in terms of age and other kinds of factors.

There are more places doing transplants, there are more transplants being done, and the criteria aren't as tight as they used to be.

So, I think just on that basis alone, people who might not have previously qualified for transplant would now qualify.

Plus, we obviously know more about the device than we did when it was put in. I mean, let's assume it was stated back when it was put in that the two most likely scenarios would be either the person would die on the table, or they may have a good long-term outcome.

Let us assume that it was not anticipated, and again, I think I agree with what Dr. Annas has repeatedly said. I don't think that there is really any kind of malice. I think everyone has good intentions. Let's assume they did not, for what ever reason, anticipate the complications, or the kinds of complications that actually occurred in Barney Clark and others.

We now know several years later that they did occur and that is really why now the permanent implantation of the artificial heart should be stopped.

Mr. **VOLKMER**. All right, and it is also my understanding that it's your position that a physician should use the left ventricular assist device, that type of thing, instead, for a bridge to transplant, rather than the artificial heart, is that correct?

Dr. **WOLFE**. Well, I think that, just to be a little more specific, the two options are a variety of left ventricular assist devices, more than two options, or the Jarvik heart. And I think that my plea really is that all of the information that has been accumulated thus far on now 21 patients who have had one or the other of those put in as bridge to transplant, all this information should be analyzed and made public so that the decision, if one of them is better, that is the one that should be given the green light.

I don't know which one will turn out better. We have a larger number of instances in which the left ventricular assist device has been used over a longer period of time. I have not seen the data, because it is kept secret.

I would love to see the data as would, I am sure, a lot of other people including the people who are operating in these difficult emergency situations on the patients. I would like to see which of these does better, if that is the case.

So, it is really let the best device be the one that is supported in terms of continuing research.

Mr. **VOLKMER**. We just recently had within this week, three operations for the purpose of the bridge. Assuming that those all lead to successful transplants, and that we continue to have others, and those lead to successful transplants, would that lead you to believe that the use of the Jarvik heart as a bridge is a valid instrument to be used in those conditions?

Dr. **WOLFE**. Well again, Dr. Jarvik and I agree that it may be a matter of not much more than luck, or whatever, as to which device is available in which city. I think that it should be something more than luck though.

And I guess, if one looks at the record of these 21 patients thus far in terms of death rate, complication rate, and everything else, one may be able to conclude that one is better than the other. And I don't know which one will turn out to be better.

Or as I said, it's possible that they will be pretty much the same. I think that whatever the data is, it needs to be made public.

And it may be in the long run that one, or perhaps two of them, or more, all have equally good results in terms of bridging people over toward transplantation.

The caveat which Dr. Annas will go into in much more detail, is, of course, this concern that we have that whenever a bridge implantation is done it may well be done in someone who otherwise might not be as good a candidate for a transplant as someone who doesn't need to have a bridge implant.

Again, that kind of data is difficult to look at and needs to be looked at.

Mr. Volkmer. Perhaps, from later witnesses—I have a question in my mind, and not being an expert in the field and not being a physician. The question arises that if this had not been available, let's assume that we did not have the Jarvik-7 available, not there. What would have been the treatment for Barney Clark, for Mr. Schroeder, for Mr. Haydon, and the others?

Dr. Wolfe. Well, in terms of at least several if not all of the people who got the permanent implant, the treatment for the small numbers of them would have been transplants. And that, in fact, is happening.

In terms of the bridge use of the device, there are, as was discussed, a variety of other devices which have been available and have been used. And I would guess that if there had not been a Jarvik-7 available, that Dr. Copeland, for example, would, if the exact circumstance or circumstances that have arisen with him, had occurred, he would have used a left ventricular assist device, one of the ones already there, as the bridge to transplant. So there are alternatives.

The alternative to the use of the Jarvik for bridge are the variety of left ventricular assist devices.

Mr. Volkmer. Does the type of heart disease, or what some of us may call heart failure in layman's terms, make any determination as to the use of which type of instrument is used?

Dr. Wolfe. It certainly does. Again, in an area that Dr. Jarvik and I would agree on, there are circumstances in which someone who has severe heart failure can benefit from the temporary use of a left ventricular assist device, which then is removed and the person doesn't really need anything, including doesn't need a transplant.

There are other people who have acute illnesses that come up that require some kind of interim device which could be a left ventricular assist device.

So, it certainly does depend on what kind of disease, whether it is a chronic, progressive worsening disease; an acute illness; and if you look at the variety of people who had implants on a permanent basis or the bridge use, you see a whole variety of different medical problems represented there.

Mr. Volkmer. Presently, even though we have an increased number of donor hearts for transplant, we still do not have enough basically to go around, do we not? And also, we have to have it, you know, within a quick period of time.

Dr. Wolfe. There is no question about that. Whether the number is 400, 500 or 600 a year, the estimates as to the number of people that need some kind of intervention are 15,000, to larger. It is that gap between the available number of transplants and those in need that has generated all this research; I don't doubt that at all.

I guess what I am saying, though, I said in the middle of the testimony; that looking down 25 years from now the best way of making that waiting list shorter is prevention.

I mean, there is no question based on what has happened thus far that 25 years from now, if we pour much more energy into the problems concerning smoking and diet, that there won't be this large number of people waiting that there are today.

In the meantime the research is obviously being pursued to come up with mechanical devices of a variety of kinds.

Most of the research is in animals, not in people, though.

Mr. VOLKMER. Therefore we get to the position that the premise of your views on the whole thing is based on that prevention is the better way to solve the problem?

Dr. WOLFE. Well, it is an additional way. Well, I mean I am not in favor of stopping all research, or even most of the research having to do with artificial assist devices totally implantable, with permanent hearts, and so forth.

I am just saying that in the long term it has been a large number of years between the time when this program was started, and now. There has obviously been some progress. We are still not close, in my view, to having a total artificial heart that can be implanted in the thousands or tens of thousands of people. In the NIH's view, they are not even going to start the experiments on that until 1994.

So, we are talking about the millennium. We are talking about 200 plus, before it is likely that this is available.

Mr. VOLKMER. But if we did nothing now but to proceed with further animal tests, where would we be?

Dr. WOLFE. Well, I mean, the plan is not just to proceed with animal tests without the possibility of human kinds of trials. I agree with the careful plan, such as the one that the NIH has now of doing the development, animal experimentation, and if that works in 1994, going on with human implantations, for that type of device.

Certainly I——

Mr. VOLKMER. Well, you have to recognize that the device itself, as I understand it from my review of materials that have been furnished me before this hearing, that the device has actually worked better in humans and for a longer period of time than it did in animals.

Dr. WOLFE. You are talking about the Jarvik heart?

Is that——

Mr. VOLKMER. Yes. The Jarvik heart.

Dr. WOLFE. And therefore what?

Mr. VOLKMER. Therefore, what can we learn further? There has already been the animal testing that we have had quite extensively.

What can we learn further from further animal testing?

Dr. WOLFE. Well, as Dr. Jarvik mentioned, modifications have been made and will continue to be made in both the Jarvik heart and others. And I think that there is definitely a role when and if such modifications are made, for doing further animal experiments to see what the impact is. Also, just the kinds of engineering experiments to look at the longevity of the materials, and so forth.

Mr. VOLKMER. The final question, I have—well, maybe not.

And it gets back to the people who have had the Jarvik heart implanted as a permanent implant. And that is your statement that they had been a candidate for a transplant.

Dr. WOLFE. Now. I mean, if these people—if we set the scene in 1986, at least several of these people now would probably get a transplant instead of the permanent implantable heart.

Mr. VOLKMER. But, if we had not had any approval for Jarvik in 1982, 1983, 1984, the people that had received the Jarvik-7 would not have had that available and——

Dr. WOLFE. My responsibility——

Mr. VOLKMER [continuing]. And your response to that was there had been a transplant.

Dr. WOLFE. Well, my response is that now, as opposed to back then—I do not know because, again, this information is kept secret, what was available then to use as the basis for the FDA approval. Let's assume that the FDA's decision then to approve permanent implantation was perfectly fine.

All I am saying is that we are now several years later and we have learned more, and now, I believe, it should be a different decision.

So, I am not questioning, although I might if I saw the data, what was decided back then.

I am just saying it is different now.

Mr. VOLKMER. Well, I have to look at the guidelines, too, as to whether or not the question was, you know, that the person wasn't a candidate for a transplant, and perhaps there wasn't availability.

Dr. WOLFE. I think that was probably——

Mr. VOLKMER. If that is the case, and if you have nothing else, you do not have the Jarvik-7 available, that person is going to die—we all know that—within a shorter timeframe, than they died with the Jarvik-7.

Dr. WOLFE. Agreed; that is why I said—my answer is questioning the continued allowing the permanent implants now as opposed to back then. I don't know what the information was available then. Let's assume that the decision was OK then, *(a)*; *(b)*, that it was more difficult because fewer places were doing them to get transplants, and for those people that was the only option. It is not the case today.

Mr. VOLKMER. Dr. Jarvik, do you wish to comment on this?

Dr. JARVIK. There are two things I wish to comment on.

And I don't understand, Dr. Wolfe, why we failed to communicate so well.

We have said and remain absolutely firm in our belief that no patient whatsoever will receive an artificial heart until every opportunity to get a transplant is exhausted. Only when no transplant is available because they are too old, because they have a medical contraindication, or because time will not permit a further search for a donor, will an artificial heart be used.

That is entirely clear. We will never use it in a situation where a transplant is available to that person.

And the other thing I would like clarify——

Mr. VOLKMER. Let me interrupt. The way it looks to me as a layman, and then you can clarify your next point, is, it's only used as an instrument of last resort, when there is no other alternative?

Dr. JARVIK. Exactly.

And regarding the question of LVAD, the patient that Dr. Griffith did recently in Pittsburgh——

Dr. WOLFE. Left ventricular assist device.

Dr. JARVIK. Left ventricular assist device—was sustained for 2 days with a biventricular assist device, both left heart assist and right heart assist. Prior to receiving the Jarvik-7 heart, this patient was not able to be maintained in a condition that they felt would allow the patient to live long enough to find a donor, with the assist device.

So, they went to the total heart.

Additionally, I agree with Dr. Wolfe that I would like to know more about the numbers of cases done with left heart assist. Many of these are not reported. I would very much like to know.

There is a system called the biomedic system that I believe has been very widely used, but there is no reporting requirement on that use, even though it is not approved for that use. And I don't quite understand why.

I think that there have been a large number of cases, and I think the only ones that we see are those that actually get to transplant. I think there have been many efforts to hold patients for transplant with heart assist devices which have failed, where they have not been able to find a donor.

In all total artificial heart cases, with every type of device that has been used, there has so far been a donor heart found for that patient. In the three that are going now we will see if those patients will be assisted long enough to find a donor.

But in the past they have always lived long enough. With LVAD there have been many that have died from other problems with the LVAD prior to finding a donor heart.

Mr. **Volkmer**. Thank you now.

And Dr. Jarvik, I would like you to, if you would be willing to do so, comment on the fact that just last week there have been several implants of both the regular and the mini Jarvik heart, under what appears to be FDA emergency guidelines or verbal approval from the FDA?

In light of what has occurred, especially in the last three, are FDA emergency guidelines unrealistic, when a doctor is faced with a real-life situation?

Dr. **Jarvik**. I believe they are. I believe that the guidelines are good guidelines, in general, regarding the first case. The only problem regarding the first use of an unapproved device is that the FDA will not permit a trained team to maintain the device in readiness.

I think that people should be allowed to have a fire extinguisher in their operating room, because situations do arise and we know it, frequently.

That is a problem, and the additional problem is that they will only allow it to be used once and say they won't approve it. And I think that we have made very clear recommendations where those guidelines, we think, can be improved, and we want to discuss that more.

I very much hope that they will adopt new guidelines or modification of the guidelines which will allow people, physicians who are trained and prepared, and have approval of their local review board, so the thing has really been thought through and approved, locally, to maintain emergency devices in readiness, and to use them in any numbers of cases that are required, while it is under review.

Mr. Volkmer. I want to make, for the record, to be clear that what we are discussing here is only for the purpose of what we call bridging, between an implant and a transplant——

Dr. Jarvik. I am sorry, I know that that may be interpreted that way, but I believe that a patient who is facing imminent death has the same right to treatment, and the physician wishes to treat that patient just as much, whether or not a bridge is permanent.

I believe an emergency situation, a true emergency here, and we are talking about a life-death condition, is a situation where that patient is going to die, and going to die quickly, and quite documentably for sure. And then, no matter what the device is, if the patient understands or the family understands in a reasonable level of detail and gives consent, be it permanent or temporary, I feel it is appropriate to use it in an emergency.

Mr. Volkmer. At the present time isn't Dr. DeVries the only physician in the United States licensed to do a permanent implant?

Dr. Jarvik. Well, under the emergency use guidelines, I believe that a permanent implant could be done at another institution. I think that the intent of those emergency guidelines was to allow physicians to try to save their patients.

I think it is very clear that patients such as Barney Clark would not be candidates, even now, under transplant criteria—you can ask Dr. DeVries if that is his same opinion—because of age and because of the severity of other medical complications.

And I think that a patient who happens to be 65 years old and is therefore excluded from transplant everywhere, who can only then have a permanent device, if they are in good enough health to do it, and if there is a team that has the resources to support them, I believe that should be done in an emergency condition as well.

You know, there is really no difference between an emergency and a nonemergency in someone who needs an artificial heart. It is always an emergency, and only an emergency.

Mr. Volkmer. Isn't the only institution that we have presently approved by FDA at Humana?

Dr. Jarvik. That is true; but in terms of the emergency guidelines, for emergency use of unapproved medical devices, those guidelines permit the first-time use of an unapproved device at any institution under a series of conditions that include the approval of the chairman of the institutional review board, and certain reporting to the FDA.

So, under those guidelines I would interpret that a permanent use could be done elsewhere.

Mr. Volkmer. Are you bascially, so I can clarify this in my own mind, talking about candidates, in other words, a person, patients, who are not candidates for a human heart transplant?

Dr. Jarvik. Absolutely——

Mr. Volkmer. That is the type you are talking about, a permanent? They would not be a candidate——

Dr. Jarvik. Absolutely. Patients who are not candidates—if a patient is not—I can give a good example. Mr. Stenberg in Stockholm was not a candidate for transplant, had been refused transplant. Some 4 or 5 months after the artificial heart his condition improved so significantly that he was again able to be considered for transplant. And he was considered for transplant; and had other complications not arisen, they may have transplanted him.

So, even a patient who is ruled out, and is called a permanent patient, if they are young enough, may be improved enough with this device to later become a candidate.

Mr. VOLKMER. Thank you.

Dr. Wolfe, do you wish to comment any further on what Dr. Jarvik has said?

Dr. WOLFE. No; I don't.

I mean other than the fact that, since only one investigator, Dr. DeVries, is currently allowed to do permanent implantations, I think, that it is sort of smearing the line.

I mean, any kind of surgery on someone who is sick, can arguably be called an emergency. I agree, but I think that that pushes too far against the definitions, at least that the FDA, I think, intends. I do not think the FDA intends to allow a whole variety of people who are not cleared to do "permanent implantation," as Dr. DeVries is, to be able to start doing these on an emergency kind of basis.

I think you can ask them to answer for themselves——

Mr. VOLKMER. I don't want to get into semantics but, again, as a layman, even in discussing this, it appears to me that perhaps the person who was given the mini-Jarvik in Texas, by Dr. Cooley and Dr. Frazier, let's assume that for some reason or other, no heart, natural heart is found. Now, is that person a permanent implant, or is that a temporary implant?

I mean, it is obvious, I am making a statement. I am not asking a question.

Dr. WOLFE. Well, I mean, one of the variables—I would imagine, again I want to keep emphasizing how important it is to look at the data on these 21, or perhaps more patients who have had left ventricular assist devices, or total hearts as a bridge. But I would imagine that one of the criteria for putting in that device may well have been the patient condition, not just the issue of availabilty of a natural transplantable heart.

So, I mean, it is possible that someone is so sick for the moment that they "aren't a candidate for transplant, but can become a candidate for transplant."

I mean, I have to see all this data. We can't keep holding all this data secret, not collecting it rigorously, and keep experimenting on people in this country, as has been done.

Mr. VOLKMER. OK, thank you.

Dr. Jarvik, I have one last question.

Now that we have had several implants on a permanent basis of the Jarvik-7—you probably have—would you comment on modifying the protocols for any future implants approved by FDA?

Dr. JARVIK. I think that we have to understand the difference between the protocol that Dr. DeVries has worked up, which I believe would be appropriate for him to comment on, because it is a very thorough, very excellent, extensive protocol, and what I believe the protocol that Symbion will support it. I believe that the work that is going to be done at Humana, that has been underway, is extremely extensive, and very costly. It is appropriate. It is excellent science.

But I do not believe that that level of extensiveness of data acquisition need be applied to all permanent artificial heart patients. I think we should have a fundamental basic assessment of performance and basic research studies that is done everywhere.

And I believe that we should have specific additional scientific studies that are done by each institution according to their resources, and interests, and special expertise, at different institutions.

So, I think that I am trying to argue for a fundamental protocol, that is appropriate, justifies it, and the option for individual scientists to study additional things.

Mr. **Volkmer**. Thank you very much, Dr. Jarvik.

Does the gentleman from Utah have any questions that he may wish to ask?

Mr. **Monson**. Thank you very much.

While not being a member of this subcommittee, I am a member of the full Science and Technology Committee, and I appreciate your allowing me to sit in with you today.

And I appreciate very much the testimony that we have heard, and the education value, and welcome Dr. Jarvik and his associates here.

I have several questions, and I think it would be appropriate if I just submitted some of them in writing if that would be appropriate, and ask them to respond——

Mr. **Volkmer**. Yes, if you would supply them to our staff, we will provide them to whoever you wish to question.

But I would like to comment to both of our witnesses, and to the witnesses in the future, that we will be holding open the record. And if there are additional questions they will be submitted to you in writing. We would appreciate your responding to those.

Mr. **Monson**. But there are a few of the questions I would like to ask here today.

We have heard a lot about the opportunities between the different bridge devices and the—assuming we use the artificial heart as a bridge device as well, and the left ventricular assist device. Are there differences enough between these that they would have different applications and suitability to patients?

Dr. Jarvik.

Dr. **Jarvik**. Yes, I certainly think so. Let me take the example of the case that occurred in Pittsburgh with a temporary assist device.

You know, I think that medical experience shows that for highly specialized procedures it is valuable to have regionalized medical centers, where certain basically more extensive procedures are done.

And as an example, a temporary left ventricular assist device which is easier to apply, might be used regionally, or broadly in hospitals around the country, community hospitals, et cetera, that could pick up a heart attack victim, could hold them over, and could allow transport of that person to a regional medical center where artificial heart surgery was done.

That would be a temporary application as a bridge to permanent total heart. That has not been really considered from that point of view, but it was done in Pittsburgh this week. And I think that there is no doubt that NIH has recognized very explicitly the need for a family of devices for different uses in different situations. There are quite a few that we need to develop for these specific applications.

Mr. MONSON. And are there situations where one or the other would not be suitable or helpful?

Dr. JARVIK. Yes; there are situations in which only one type of device would be appropriate for that patient and other types of devices would be inappropriate for that patient.

Mr. MONSON. Dr. Wolfe, do you have a comment on that?

Dr. WOLFE. Well, I mean, let us agree that there are different circumstances for the application of even different left ventricular assist devices, aside from left ventricular assist devices as a family versus the implantable heart.

But I think that to use Dr. Jarvik's phrase again, it should not be a matter of luck, but really a matter more of planning as to which ones are available at a reasonable level. And it also should be a matter of looking at the record of them in the various circumstances in which they have been used.

We need to compare the use in similar circumstances when there are data on that. All of that again bespeaks the need to analyze every single circumstance in which either of these has been used on a bridge basis.

Mr. MONSON. With regard to some of the statements that were made regarding the compatibility with blood cells and such, with the materials used in building the total artificial heart, you referred in your response to some of my colleague from California's questions, to Mr. Packard, to what might occur around the valves and such. But what about your response to other aspects that were not brought out with regard to whether or not the materials are compatible with blood cells, et cetera?

Dr. JARVIK. Yes; I am sorry, I didn't complete the answer to Mr. Packard's question.

We have found in the longest Jarvik-7 heart that has pumped in a human being, the heart in Mr. Stenberg, and we analyzed that in great detail; we found no indications of degradation of the material, especially by calcification. It was completely free of calcification. In a calf at that point it would have been highly calcified.

And we found that very encouraging. We do a lot of analysis of the heart and the materials. And we believe at this point that these materials show very little, if any, degradation in long-term contact with the blood.

So, we think we have a system with a high probability of being stable in blood without chemical interactions that are damaging to the blood for long periods of time. And I mean in excess of 5 years.

Mr. MONSON. So, it works both ways, it doesn't damage, to the best of your——

Dr. JARVIK. Neither do we believe that the blood seriously damages the material; nor do we believe that the material seriously damages the blood.

Mr. MONSON. Thank you very much.

Dr. WOLFE. Can I just kind of briefly comment on that, please?

If one goes back to the element of the artificial heart called the valve. I mean, we have a fair amount of history on heart valve implantations alone, artificial ones, and in the last 10 or 15 years before, the so-called natural ones, or porcine ones, pig valves.

I don't think there is any question that just at the level of looking at the valve, it is more likely to have clotting problems with the artificial ones, an individual artificial valve implanted, than with the natural or pig valve. The artificial heart is not one valve, it is multiple valves, as Dr. Jarvik demonstrated a few minutes ago.

So, I think that, whereas in the ideal circumstance he and I would both like to have such devices lined by natural components, the intima, the endothelial cells—and that may eventually happen, I mention this exciting research at least at the blood vessel level—in 10 or 20 years, if we don't have that, we are likely to have a material that is more biocompatible.

I think the statement that the material doesn't degrade is probably accurate. Again, we don't have access to all data. But I think that it cannot be denied that the use of, at least, the presently available artificial materials has a greater risk of causing blood clots than the natural materials.

That is just the way it is, I am afraid. And maybe we will get closer than we are right now. But——

Mr. Monson. I think that we would all agree that the future holds in store some wonderful things for us, and we anxiously look forward to that time when we can take advantage of those things. But we have to deal with what we have now, too, and recognize that we have to do the best that we can with what we have now and not always live for the future, at the risk of——

Dr. Wolfe. I was simply commenting on the fact that I think that it is not accurate to say that there is no difference. I don't think that Dr. Jarvik said that at all, but I think we should realize that there is a difference in the tendency, particularly around the area of the valves, of an artificial heart to cause blood clots as opposed to a perfectly natural one. That is all.

Mr. Monson. Dr. Jarvik, do you believe that the FDA has been reasonable in its regulation of the artificial heart, and especially in light of the imposition of time requirements that you can only do one every 3 months, or something like that? Is that a reasonable approach to this?

Should time constraints like that be put on?

Dr. Jarvik. Well, I believe that the FDA has given this a tremendous amount of thought and attention, and I believe that the amount of attention they have given, given the small number of patients that are treated and the small number that could be treated even if we had no regulation whatsoever at this point, they have given it an inordinate amount of energy and attention compared to a lot of other pressing needs at FDA.

I think that they have made every effort to evaluate the information to lead to a good outcome.

And as I said in my prepared remarks, I think the difficulty that they have evolves around the fact that they have been held responsible by the law to assess risk/benefit ratio.

And they are trying to find, I think, have tried to find a line about when is a risk of complication too great, and therefore you should deny the heart to a patient who would otherwise die.

And as I said, I think the law should not require that decision to be made by the FDA. If the law were different I think it would have been a lot easier for them to deal with the matter.

And I wish that it had allowed some more rapid use, and I wish that we had had approval at some additional medical centers for permanent use.

And we will now present additional data as we gain more data, and I hope that in the near future we will get approval to do it more broadly.

So I think that, as I said, I think that in the context of the life and death situation, this need not be regulated as heavily as it has been.

Mr. MONSON. Thank you very much.

Mr. Chairman, I thank you again for allowing me to participate; and I will submit the rest of my questions in writing.

Mr. VOLKMER. Thank you very much.

And I too, wish to thank this panel for your very informative testimony.

Dr. Jarvik, I wish to congratulate you and your predecessors in the work you have done to bring this to this point in the medical field in regard to the artificial hearts and devices; and I think you are to be commended for that.

And, Dr. Wolfe, I sincerely thank you for your testimony because it gives us a little different viewpoint as to the whole thing, and I think that is really necessary in order to continue the realm of looking at the full picture as to where we're going.

Thank you very much.

You two witnesses are permanently excused; and thank you.

Mr. VOLKMER. Our next panel—and by the way before we proceed with the next panel, I would like to announce that we will proceed with the testimony from the next panel. Following that, we will recess for 45 minutes for lunch and then we will come back with the second panel for questioning.

The next panel is Mr. Mel Schroeder, family member, artificial heart recipient; Dr. George Annas, professor of health law, Boston University Schools of Medicine and Public Health; and Dr. William C. DeVries, Artificial Heart Program, Humana Heart Institute International.

I would like to proceed with testimony of Mr. Schroeder.

I have reviewed your testimony, as well as, the rest of them, and just like the previous panel all of your testimony that you have submitted in writing will be made a part of the record at this point in the record; and you may either summarize or review your testimony in full, however you so desire.

We will start with Mr. Schroeder.

And I personally want to thank you for being here, sir.

STATEMENTS OF MEL SCHROEDER, FAMILY MEMBER, ARTIFICIAL HEART RECIPIENT, FERDINAND, IN; DR. GEORGE ANNAS, J.D., M.P.H., EDWARD R. UTLEY, PROFESSOR OF HEALTH LAW, BOSTON UNIVERSITY SCHOOLS OF MEDICINE AND PUBLIC HEALTH, BOSTON, MA; AND DR. WILLIAM C. DeVRIES, ARTIFICIAL HEART PROGRAM HUMANA HEART INSTITUTE INTERNATIONAL, LOUISVILLE, KY

Mr. **Schroeder**. Well, thank you very much; I am happy to be here.

I got a letter from Doctor Glowinski on some of the protocol here. In it she indicated that I had about 10 minutes to give an oral speech.

Mr. **Schroeder**. I am only going to be talking for about 10 minutes here, so everybody that is hungry they can get out and get something to eat.

My name is Mel Schroeder, and I am the eldest son of the second artificial heart implant patient, William J. Schroeder. My mother, my three brothers, my two sisters, along with myself have been alongside my father in the past 14 months, experiencing life with an artificial heart implant.

My father was a military person with 14 years in the U.S. Air Force, and 17 years civil service at the Crane Ammunition Depot in Crane, IN. He was a very energetic and determined person, always full of life.

His health started deteriorating about 1 year before the artificial heart implant. And like many Americans today, my father experienced heart problems resulting in a sudden heart attack.

He was hospitalized and followed the standard medical procedures for heart treatment. It was determined that a coronary artery bypass graft was required and this procedure was performed, and everyone hoped that he would be able to lead a normal life, with the limitation of reduced activity.

However, his condition continued to become progressively worse, leading to another heart attack. At this point, the doctors informed everyone he was critically ill and would have 4 to 6 months to live at best.

The months leading to his second heart attack were not without weakness, pain, and constant breathlessness. And the months before the implant were even worse.

But dad was a very determined person, and he was not willing to give up and die. He asked the doctors what could be done. A human heart transplant was ruled out because of a diabetic condition and age. Being backed into a corner, the only remaining choices were the artificial heart or certain death.

With my father's determination, his desire to continue to experience life for events such as a son's wedding, the first Schroeder grandson, hopefully, returning home to a life with his family, along with the possibility that he may be able to help other people, and his admiration for Dr. DeVries, and his medical staff, dad chose life and the artificial heart.

This picture depicts a person near death reaching for some hope, any hope to continue living. For 2 weeks medical tests were taken to determine if dad was a suitable candidate.

These 2 weeks included removal of upper teeth, due to infection, and a gallbladder operation, along with various medical tests required. The review process was very thorough, with some 20 doctors' involvement.

In my visits it became more and more evident that he was preparing himself for this operation, and was very determined to go through with it. I believe in his mind, it was made up before we ever saw a consent form.

The family all supported him and the medical staff; and we still do today.

But everything was moving so fast and everyone was caught up in the situation at hand, that we hadn't discussed in detail the possible medical complications; and to this, it is my only regret that we as a family did not sit down with dad and discuss how we were going to, and how dad would want us to handle situations that might arise.

In looking back I believe it is tremendously important to insist, for a family to determine what their roles would be from the onset; and not only become aware, but understand any complications that may occur.

I am not saying that this discussion would have changed our minds about the artificial heart. But I believe it would have made us more prepared.

Dad's initial success astounded everyone, including myself. His power and colorful personality became an inspiration for people everywhere. Cards and letters by the hundreds came pouring in from well-wishers, many from people which had experienced similar heart problems themselves.

It had been months since I had seen him with so much energy, joking, and smiling all the time. I remember one evening while still in the CCU, dad was recalling some of his jokes to the hospital personnel in the room.

But being a true Democrat I believe most of his jokes were about Republicans. The laughter became so intense that the nurses at the desk had to knock on the door and ask everyone to hold the noise down, that we were disturbing the other patients.

But for nearly 3 weeks he continually improved from day to day. And then the day came, and dad was struck by his first stroke.

What everyone had hoped for was now set back for an undetermined amount of time. It is at this point that we first realized what a stroke actually was.

We had heard of the affliction, but did not know what all was involved. In the months to follow we became more and more familiar with the limitations associated with the stroke.

You might say that we became educated as each day passed. We became more familiar with the artificial heart support equipment, and maneuvering with dad and the equipment.

And, as a family that was proud of and loved our father, we became more involved with his daily activities. The year ahead would be plagued with medical complications, but as a family together with many devoted persons, we managed to make a year of possible tragedy become a part of all our lives which we will cherish forever.

We focus on the good times which would never have happend without the artificial heart implant.

I can remember the holidays of Christmas and Thanksgiving were always a special family time. My brother's wedding reception; the stroll through the park with his grandchildren; the baptism of the first Schroeder grandson, and being able to hold the baby; the fishing trips; the rides in the customized van; the Louisville Red Bird Minor League Baseball Team game; and the trip back home to participate in a parade, with thousands of people lining the streets and giving him a standing ovation.

These were some of many situations that a stroke patient with an artificial heart was capable of participating in.

Of course, with the good times we also experienced the bad.

There were times we were torn apart from the complications which arose. We were continually saddened by additional strokes.

The frustration ruined many days, which found us helpless. Stress and exhaustion were frequently present. There is no doubt that they were very rough situations to endure.

And although at times there, it was very difficult to laugh and a hidden fear could be felt, we were still holding on to a smile for a brave father who we all loved so very much.

A question which has always been in the foreground, and asked by any reporters that I have spoken to is: Is it all worth it?

Well, that seems to be a very difficult question to answer. But I do realize that this question is usually forgotten when the many happy times were present.

Everyone would have a different value for what it would be worth to see and hold their grandson. Of course, these events are few, and I would really have no way to determine which way the scale would lean. But looking back, I realize my father, William Schroeder, is truly a pioneer; he has accomplished many firsts for mankind.

He was the first artificial heart implant to go outside of the hospital, the first to use a portable drive system, the first to ride in a vehicle, the first to attend a public gathering, the first to live outside the hospital, the first to return to his home, some 90 miles from the hospital.

And he was also the first person to get overnight acceptance to the Social Security Program. And all of these firsts were accomplished by a stroke patient with an artificial heart.

I wonder what other firsts could have been accomplished if other complications were removed?

But paying for these firsts took hard work and devotion. And there was an idea of what would be required, but with no past record to compare, new protocols had to be established.

These protocols had to be improved on as different situations and questions arose. I can't say that I agree with everything in the past year, but I do believe that many things have been learned and many can and will be improved on.

As each situation is experienced, more information is gathered which can be used to help the next implant. The Schroeder family is willing to provide any insight to persons and families considering an artificial heart implant for a bridge or a permanent use.

You know, last Tuesday I learned of the tragedy of seven American astronauts, and grieved with the Nation for all their families. As I thought of what they might be experiencing, I could somehow, somewhat, relate to what they might be going through.

Everyone feels for these pioneering people, we all remember their courage to put the advancement of mankind before their own lives.

You recall and hold on to the success you have experienced; you praise the pioneers of technology and dream for the future success of mankind. This holds true for all technologies. There is a long way to go and many problems and questions to be answered with the artificial heart program.

But with pioneers like my father, William Schroeder, you get closer everyday.

Thank you very much.

[The prepared statement of Mel Schroeder follows:]

WRITTEN STATEMENT TO THE
SUBCOMMITTEE ON INVESTIGATION AND OVERSIGHT
OF THE
COMMITTEE ON SCIENCE AND TECHNOLOGY

BY

MEL SCHROEDER
FEBRUARY 5, 1986

BIOGRAPHY

MY NAME IS MEL SCHROEDER, ELDEST SON OF WILLIAM J. SCHROEDER, 2ND ARTIFICIAL HEART IMPLANT. I AM 31 YEARS OF AGE, MARRIED OF 11 YEARS AND HAVE 2 CHILDREN AGES 6 & 8. I LIVE IN A RURAL AREA OF A SMALL TOWN OF FERDINAND, INDIANA. I AM A GRADUATE OF A JUNIOR COLLEGE, VINCENNES UNIVERSITY IN INDIANA WITH AN ASSOCIATE DEGREE IN ELECTRONIC TECHNOLOGY. I AM EMPLOYED AT KIMBALL INTERNATIONAL RESEARCH AND DEVELOPMENT DIVISION FOR 11 YEARS AS AN ASSOCIATE ENGINEER. I HAVE BEEN THE SPOKESPERSON FOR THE SCHROEDER FAMILY OVER THE PAST YEAR AND HAVE APPEARED ON MANY NEWS SHOWS AND PUBLIC GATHERINGS. I ENJOY OUTSIDE ACTIVITIES AND ALL SPORTS

PLEASE FIND ATTACHED A SPEECH GIVEN BY MYSELF TO THE AMERICAN FOUNDATION OF COMMUNICATIONS IN WASHINGTON D.C. ON OCTOBER, 1985. THIS SPEECH SUMMERIZES THE FAMILIES EXPERIENCES OVER THE LAST YEAR. I HOPE THIS DOCUMENT WILL GIVE SOME INSIGHT TO A FAMILIES PERSPECTIVE OF THE ARTIFICIAL HEART PROGRAM.

THANK YOU JACK
I WOULD LIKE TO THANK THE FOUNDATION OF AMERICAN COMMUNICATIONS FOR ASKING ME TO BE A SPEAKER AT THIS CONFERENCE ON THE ARTIFICIAL HEART. IN PARTICULAR I WOULD LIKE TO THANK SANDY BLAKELEE WHO CONTACTED ME AND ALL OF YOU PEOPLE FOR LENDING AN EAR. I FEEL HONORED TO BE ASSOCIATED WITH SOME OF THE LEADING DOCTORS, INVENTORS AND PRESS PERSONS IN THIS FIELD. I UNDERSTAND THAT MANY OF THE LEADING SURGEONS IN THE ARTIFICIAL HEART FIELD ARE HERE FOR THIS CONFEREENCE. I BELIEVE I READ WE HAVE DRS. COPELAND, SEMB,JARVIK,COOLEY, FRAZIER, DEVRIES AND I DO BELIEVE WHEN WE WERE CHECKING IN EARLY WE CAUGHT A GLIMPSE OF THAT FAMOUS DOCTOR, I BELIEVE HE IS KNOWN AS TRAPPER JOHN. DR JOHN DID THINGS A LITTLE DIFFERENTLY THEN MOST DOCTORS. FIRST HE BECAME A T.V. PERSONALITY AND THEN HE BECAME A DOCTOR. MAYBE THAT IS THE WAY TO GO BECAUSE I SURE THAT HE HAD AN EASIER TIME THEN I REMEMBER.

AS JACK SAID MY NAME IS MEL SCHROEDER SON OF ONE OF THE BRAVEST MEN I KNOW, BILL SCHROEDER. I AM SURE I HAVE MET ALOT OF YOU PEOPLE AND MANY OF YOU MIGHT REMEMEER ME. HOWEVER I'M SURE MANY HAVEN'T HAD THE OPPORTUNITY AND IT SEEMS MOST HAVE A HARD TIME DISTINGUISHING BETWEEN MY BROTHERS AND MYSELF. SO MUCH , THAT I'VE I FELT PERHAPS AN AMERICAN EXPRESS CARD MIGHT HELP. UNFORTUNATELY THE PROBLEM OF BEING CONFUSED WITH MY BROTHERS STILL REMAINS AND NOW I HAVE ANOTHER MONTHLY BILL AND MORE JUNK MAIL.

TO TELL YOU THE TRUTH THIS IS THE FIRST TIME I HAVE HAD AN OPPORTUNITY TO BE A SPEAKER IN FRONT OF SUCH A GROUP OF PEOPLE. I'M USED TO THE TELEPHONE INTERVIEWS IN WHICH I WAKE UP THE NEXT MORNING AND RUSH TO SEE WHAT I REALLY SAID. I MUST ADMIT IT IS QUITE DIFFERENT AND I AM SOMEWHAT NERVOUS. I HAD TO DO ALOT OF PREPARATION FOR THIS TALK. I SPENT SEVERAL NIGHTS WATCHING VIDEOS OF SOME PROMINENT MEDICAL FIGURES SPEECHES. FROM THESE SPEECHES I REALIZED TWO THINGS YOU NEED TO BE A SUCCESSFUL MEDICAL SPEAKER. NUMBER ONE YOU HAVE TO WEAR A WHITE DOCTORS COAT OR SCRUBS WITH THE CUTE LITTLE HATS. WELL I DIDN'T WANT HUMANA KNOWING THAT I HAD BORROWED ATTIRE FROM THEIR PERSONNEL COLLECTION. SECOND YOU MUST HAVE THE ABILITY TO TALK FOR 20-30 MINUTES USING MANY UNPRONOUNCIBLE MEDICAL TERMS. THIS INSURES TO THE AVERAGE LISTENER THAT YOU REALLY KNOW WHAT YOU'RE TALKING ABOUT EVEN THOU THEY HAVE NO IDEA.

THERE ARE SO MANY THINGS I COULD TOUCH ON TONIGHT BUT I HAVE LIMITED THEM DOWN TO A FEW. SINCE I HAVE AN INSIDE TRACK ON AN ARTIFICIAL HEART PATIENTS FAMILY, I THINK I WILL TOUCH ON THAT A

LITTLE. I WOULD ALSO LIKE TO GIVE A LITTLE ADVICE TO THE SURGEONS AND THE REPORTERS. I WOULD LIKE TO INJECT A SMALL NOTE ON THE FUTURE OF THE ARTIFICIAL HEART AFTERWHICH I HOPE TO BE AT THE CONCLUSION.

FIRST LET ME BEGIN BY TELLING YOU A LITTLE ABOUT THE LAST YEAR AND A HALF OF THE SCHROEDER FAMILY. IT ALL STARTED IN THE SPRING OF 84. I WAS SLEEPING, IT WAS ABOUT 3 IN THE MORNING AND THE PHONE RANG. IT WAS MY BROTHER TERRY. THERE WASN'T ANY BEATTING AROUND THE BUSH HE SIMPLE SAID, DAD HAD A HEART ATTACK. FROM THAT NIGHT WE HAVE TRAVELED ALONG SIDE DAD THROUGH A DOUBLE BY PASS, GULL BLADDER OPERATION, AN ARTIFICIAL HEART IMPLANT AND A SERIES OF STROKES.
WE HAVE GONE FROM A FAMILY WHICH WAS TIGHTLY BOUND LIVING A NORMAL UNEVENTFUL LIFE TO A FAMILY WHICH HAS GAINED NATIONAL ATTENTION OVER NIGHT.

THROUGHOUT THIS PERIOD WE HAVE BOUNCED FROM EMOTIONS OF EXCITED, HAPPY,AND HOPEFUL TO FRUSTRATED, SAD, ANGRY, AND HELPLESS. WE HAVE LAUGHED TOGETHER AND WE HAVE CRIED TOGETHER. IT HASN'T BEEN THE EASIEST OF TIMES. BUT THESE TIMES HAVEN'T BEEN WITHOUT REWARD. I CAN RECALL THE MANY HUNDREDS OF PEOPLE UNKNOWN TO US THAT SENT WELL WISHES AND WORDS OF THANKS FOR GIVING THEM ADDITIONAL STRENGTHS TO CARRY ON. I REMEMBER THE WEEKS AFTER THE IMPLANT WHERE DAD WAS BETTER THEN I HAD REMEMBERED FOR MONTHS. I REMEMBER THE HOLIDAYS AND OUTINGS WE SPENT AS A FAMILY.I REMEMBER ALL THE PEOPLE THAT WERE MORE THEN KIND, AND I REMEMBER AND CHERISH ALL THE NEW FRIENDS WE HAVE ACCUMULATED.

ALONG WITH THE GOOD YOU ALSO HAVE THE BAD.I REMEMBER THE STRUGGLE DAD WENT THROUGH TO BREATHE BEFORE THE IMPLANT. I REMEMBER THE EMPTY FEELING LIKE SOMEONE TOOK THE FEET FROM UNDER YOU WHEN HE RETURNED TO THE OPERATING ROOM DUE TO EXCESSIVE BLEEDING. I REMEMBER THE NIGHT I RECEIVED THE PHONE CALL TELLING ME DAD HAD A STROKE, AND I REMEMBER THE EFFECTS OF THE STROKE. I REMEMBER THE WEDDING HE WAS UNABLE TO ATTEND. I REMEMBER THE FRUSTRATION HE WAS AND IS EXPERIENCING ON THE ROAD BACK. IN ALL THESE SITUATIONS WE SHARED THEM WITH MOST OF YOU AND THE WORLD.

ALMOST ONE YEAR LATER AND WE ARE STILL FIGHTING FOR LIFE. THE QUESTION ARISES HOW DO YOU COPE WITH IT. THE IMPORTANT THING IS TO MAKE SURE THAT YOU YOURSELF GROW DURING THE SITUATION AND NOT LET THE SITUATION GROW ON YOU. I HAVE A SIMPLE PHILOSOPHY AND THAT IS

YOU DO ALL YOU CAN AND NO MORE. UNFORTUNATELY THAT IS SOMETHING EASIER SAID THEN DONE. IT IS EASY TO PUT YOURSELF IN THE POSITON AND BEAT YOU HEAD AGAINST WALL TRYING TO HELP WHERE YOU ARE HELPLESS. THE IMPORTANT THING IS TO DETERMINE WHAT YOU CAN DO AND THEN TRY AND DO IT. YOU CAN'T DO IT ALL AND YOU SHOULDN'T TRY. THE ONLY THING THAT IS WORSE THEN 1 PERSON BEING HOSPITALIZED IS 2.

WHEN WE FIRST KNEW OF DAD'S PLANS FOR AN ARTIFICIAL HEART, EVERYONE KNEW THAT WE WOULD BE IN THE EYES OF THE PUBLIC, BUT WE DIDN'T KNOW EXACTLY WHAT THAT CURTAILED. WE WERE REALLY AWAKEN THE NIGHT THE NEWS WAS RELEASED. THE PHONE RANG CONSTANTLY. PEOPLE WERE KNOCKING ON THE DOORS FRONT AND BACK. THE STREETS WERE LINED WITH REPORTERS.

I REMEMBER THE NEXT MORNING SOMEONE GOT UP AND OPENED THE DOOR FOR THE PAPER. A SERIES OF CAR DOORS OPENED WITH REPORTERS AND CAMERA CREWS JUMPING OUT. IT WAS QUITE COLD THAT NIGHT. EVERYTIME SOMEONE NEW GOT UP WE WOULD OPEN THE DOOR AND SHUT IT AGAIN TO SEE HOW MANY PEOPLE WOULD OPEN THEIR CAR DOORS. IT WAS REALLY KIND OF FUNNY.

THE BAD THING ABOUT THE PRIVACY ISSUE WAS THAT EVERYTIME YOU DID ANYTHING WITH DAD THAT WAS SOMEWHAT SIGNIFICANT THE STORY WAS OUT AND YOU HAD TO MAKE ROOM FOR THE PRESS. YOU ALSO HAD TO MAKE ROOM FOR SECURITY, TECHNICIANS, NURSES AND VERIOUS HOSPITAL PERSONAL. I DON'T BLAME ANYONE IT WAS THEIR JOB AND I'M SURE THAT IT WAS NEWS THAT A LOT OF PEOPLE WERE INTERESTED IN. I WISH THAT IT COULD WORK OUT WHERE WE COULD DO SOMETHING AND THEN RELAY THE INFORMATION TO THE PRESS BUT I CAN'T SEE HOW THAT WOULD HAPPEN WITH ALL THE COMPETITION. BASICALLY THE PRESS AS HANDLE THEMSELVES PRETTY WELL. WE HAVEN'T HAD MANY PEOPLE PEERING IN WINDOWS AND NO HAD TO HIT ANYONE TO GET THEIR ATTENTION. BUT IT IS KIND OF LIKE HAVING A PARTY AND SOMEONE SHOWS UP WHICH WASN'T INVITED. WHEN PLANS ARE BEING MADE FOR AN EVENT ONE OF THE FIRST THINGS THAT COMES UP IS HOW DO YOU HANDLE THE PRESS. THE BOTTOM LINE IS THAT YOU HAVE TO GIVE THEM SOMETHING TO REPORT. IF MY FATHER WAS WELL AND CAPABLE THIS MIGHT NOT BE AS MUCH A PROBLEM. AS YOU CAN PROBABLY REMEMBER HE WASN'T AFRAID TO BRING UP ANY ISSUE. IF YOU DON'T BELIEVE ME YOU CAN GO 2 BLOCKS DOWN AND ASK MR. REAGAN.
TO ANYONE WHICH IS GOING THROUGH A HISTORICAL MEDICAL PROCEDURE, I SAY BE PREPARED. IF IT IS NEWS, YOU WILL HAVE PLENTY OF ATTENTION WHETHER YOU WANT IT OR NOT AND I DON'T SEE THAT CHANGING IN THESE

UNITED STATES. YOU SHOULD DETERMINE FROM THE START HOW YOU AS A FAMILY WANT TO HANDLE IT. IS ONE PERSON GOING TO BE THE SPOKES PERSON ARE YOU GOING TO LEAVE IT TO THE DOCTORS OR JUST HOW ARE YU GOING TO HANDLE IT. YOU HAVE TO ADDRESS THE ISSUE BECAUSE IT WILL ALWAYS BE THERE.

I WOULD LIKE TO GO ON TO MY LITTLE ADVICE TO THE SURGEONS. I HAVEN'T HAD AN OPPORTUNITY TO MEET ALL THE SURGEONS HERE TONIGHT BUT I WOULD LOOK FORWARD TO IT LATER. THE ONE DOCTOR I SEE MORE THEN ANYONE OF COURSE IS DR. DEVRIES. AND LET ME SAY OUT FRONT THAT I REALLY LOOK UP TO THE MAN OF COURSE BEING ONLY 5'9 I LOOK UP TO MOST OF HIS FAMILY. WE HAVE INCLUDED HIM IN OUR FAMILY AND WILL ALWAYS BE GRATEFUL TO EVERYTHING HE HAS DONE.

THERE ARE 2 THINGS WHICH I SEE WHICH MAY MAKE LIFE ALOT EASIER FOR FUTURE ARTIFICIAL HEART IMPLANTS THE FIRST IS INFORMATION. THE PATIENT ALONG WITH THE FAMILY HAS THE RIGHT TO KNOW WHAT ALL THE POSSIBILITIES ARE IN DETAILS. THEY NEED TO KNOW EVERY BIT AS MUCH AS THE PATIENT AND POSSIBLE MORE. THEY NEED TO KNOW WHERE THEY FIT IN, HOW MUCH IS TO BE REQUIRED OF THEM AND WHAT PLAN IS MADE IN CASE SOMETHING GOES WRONG. IN OTHER WORDS PUT EVERYTHING OUT ON THE TABLE. HAVE A DOCUMENT THAT THE FAMILIES CAN READ AND SIGN SAYING THEY UNDERSTAND THE RISKS. ONCE ALL THE INFORMATION IS READ AND UNDERSTOOD IT IS IN THE BEST INTEREST OF THE FAMILY FOR THEM TO DETERMINE HOW THEY ARE GOING TO HANDLE EVERYTHING WHETHER IT BE GOOD OR BAD.

ONE OF THE PROBLEMS WITH THIS IS SOMETIMES YOU DON'T HAVE THE TIME TO SPEND DAYS DETERMINING HOW EVERYTHING SHOULD BE HANDLED. BUT THE QUESTION ISN'T WHETHER YOU WOULD HAVE DONE IT OR NOT. IT IS A QUESTION OF UNDERSTANDING EACH OTHER AS A PATIENT, FAMILY AND DOCTOR. IF YOU KNOW WHAT MIGHT HAPPEN AND WHAT CORRECTIVE ACTIONS WILL TAKE PLACE BEFORE HAND, YOU CAN DEAL WITH IT MUCH BETTER LATER.

NOW MOVING ON TO THE REPORTERS. I REALLY WOULD LIKE TO MEET EVERYONE HERE JUST TO SAY HELLO AND ASK YOU JUST HOW YOUR FATHER AND MOTHER ARE DOING TODAY. THE ONLY ADVICE I HAVE TO GIVE TO YOU IS IF YOU'RE IN A PINCH AND YOU CAN'T THINK OF ANYTHING ELSE TO WRITE ABOUT, DO SOMETHING ELSE THEN INACCURATE STORIES ABOUT THE ARTIFICIAL HEART IMPLANTS AND FAMILIES. WE FOUND OUT MANY THINGS WE DIDN'T KNOW ABOUT OURSELVES. FOR INSTANCE, MY MOTHER NOW IS A

DIABETIC, I RANGE IN AGE FROM 28-32, MY FATHER IS PARALYZED FROM THE NECK DOWN, I WAS GIVEN CREDIT FOR BEING THE FATHER OF MY BROTHERS BABY AND THE LIST GOES ON.

THERE ARE ALWAYS A FEW BAD APPLES IN THE BUSHEL WHICH PUSH TO GET A LITTLE CLOSER, BUT IN GENERAL I WOULD SAY WE HAVE GOTTEN ALONG PRETTY WELL. IT IS JUST I DON'T BELIEVE EVERYTHING I READ ANYMORE.

I HONESTLY BELIEVE THAT NO ONE REALLY WANTS TO HAVE AN ARTIFICIAL HEART IMPLANT , A HUMAN HEART TRANSPLANT,OR A HEART BY-PASS I THINK THEY WOULD RATHER KEEP THEIR OWN. UNFORTUNATELY THEY WOULD DIE IF THEY DID. THE ARTIFICIAL HEART PROGRAM IS WIDE OPEN WITH TREMENDOUS POTENTIAL. I DON'T BELIEVE WE ARE NEAR THE FINAL STAGES BUT RATHER APPROACHING THEM MORE AND MORE AS MORE IMPLANTS TAKE PLACE. NEW IDEAS, NEW DESIGNS, NEW MEDICINES BRING WAY FOR POSSIBLE SUCCESS. SOMEWHERE DOWN THE ROAD I BELIEVE ALL THE INFORMATION GATHERED TODAY WILL LEAD TO A ARTIFICIAL HEART WHICH MORE AND MORE PEOPLE CAN ACCEPT AND BE COMFORTABLE WITH. I DON'T BELIEVE YOU WILL GET A LARGE PERCENTAGE OF PEOPLE THAT ARE WILLING TO LIVE THEIR REMAINING LIVES ATTACHED TO A 350 LB MACHINE EVEN IF NO OTHER MEDICAL PROBLEMS OCCUR. THIS PROCEDURE AND WAY OF LIFE IS NOT FOR EVERYONE . IT TAKES A SPECIAL PERSON WITH A WILL TO LIVE TO CHOOSE THIS ROUTE AND I SALUTE EVERYONE OF THEM. IT ISN'T WHAT IS BEING DONE TODAY BUT WHAT MIGHT BE ACCOMPLISHED TOMORROW.

I BELIEVE FOR THE PROGRAM TO BE SUCCESSFUL IN THE FUTURE YOU WILL SEE SMALLER DRIVE SYSTEMS PORTABLE FOR LONGER PERIOD OF TIMES, AND THE TOTAL ELIMINATION OF STROKES. BASICALLY, THE PERSON SHOULD BE ABLE TO THINK, WALK, TALK AND BE PRODUCTIVE IN SOCIETY.

WELL I WOULD LIKE TO GET TO THE HEART OF MY MESSAGE AT THIS TIME. FIRST I WOULD LIKE TO EXPLAIN A LITTLE WHY I DECIDED TO COME TO THIS CONFERENCE. I AM SURE THERE ARE PEOPLE WHO WONDER WHY I AM NOT SPENDING THESE DAYS WITH MY FATHER INSTEAD OF COMING TO GLAMOUROUS WASHINGTON D.C. WELL IT IS A GOOD QUESTION AND DESERVES AN ANSWER. AND THAT IS I BELIEVE THAT ALL THESE PEOPLE ASSOCIATED WITH THE ARTFICAIL HEART ARE TRYING SOMETHING WHICH IS VERY DIFFICULT THEY ARE TRYING TO PRESERVE LIFE. IN THESE DAYS OF MILITARY MIGHT, WITH EQUIPMENT DESIGNED TO KILL PEOPLE, I AM GLAD TO SEE THAT THERE STILL ARE SOME PEOPLE WELLING TO WORK FOR LIFE. I AM NOT SAYING THAT EVERYTHING THEY HAVE DOME COULDN'T BE IMPROVED ON OR THAT THEY WERE ALWAYS RIGHT I AM NOT SAYING THAT THERE ISN'T

ROOM FOR IMPROVEMENT. I DON'T KNOW THE ANSWERS TO THE QUALITY OF LIFE, THE FINANCIAL EHTICS OR LEGAL QUESTIONS. BUT I DO KNOW THAT IF NO ONE TRIES NOTHING IS GAINED. I WISH THAT MY FATHER DIDN'T HAVE 2 STROKES, BUT THAT WASN'T TO BE. I AM SURE AS I AM STANDING HERE IF HE HADN'T AND HE WAS AS WELL AS HE WAS 2 WEEKS AFTER THE SURGERY HE WOULD BE STANDING HERE TONIGHT GIVING THIS SPEECH. I BELIEVE A FAMILY PROSPECTIVE NEEDED TO BE PRESENTED AND I HOPE THAT I WAS CAPABLE ENOUGH TO REPRESENT DAD AND MY FAMILY. WE HAVE ALL COME A LONG WAY AND WE ARE ALL VERY WEARY. STILL LIFE GOES ON. IN CLOSING I WOULD LIKE TO SAY THAT SOMETIMES YOU HAVE TO KEEP LAUGHING OR YOU MIGHT START CRYING AND SOMETIMES YOU HAVE TO CRY BEFORE YOU CAN START LAUGHING AGAIN.

Mr. **Volkmer**. Thank you, Mr. Schroeder.

Dr. Annas.

Dr. **Annas**. Chairman Volkmer, my name is George Annas, and I am a lawyer and professor of health law at Boston University Schools of Medicine and Public Health.

I want to thank you for inviting me to address the legal and ethical issues involved in artificial heart experimentation today. And what I plan to do is just to hit the main issues, summarize my testimony, and, as I understand, the entire testimony will be in the record.

Artificial heart implants represent the most public human experiments in the history of the world, and the manner in which they are conducted is a matter of utmost public concern since it graphically portrays the seriousness with which we take our laws and ethical rules regarding the protection of the rights and welfare of human subjects.

My general view is that ethics and law have taken a distinctly back seat to notions of scientific advance; that artificial implant experimentation is being conducted almost in an historic vacuum with scant regard for existing norms and codes of human experimentation.

NIH and FDA have been unable or unwilling to supervise or control implant experimentation. And that, therefore, additional steps must be taken to safeguard the rights and welfare of human subjects of future implant experimentation.

Before I outline the reasons for these disturbing conclusions, let me first emphasize that I don't question the motives of any of the players in this drama. Indeed, in the arena of human experimentation, all involved have different and appropriate social roles.

But the roles of inventors, researchers, and surgeons do not exhaust the universe. In dealing with human experimentation you are dealing with an area which involves public values which are crystalized, in our view, of the rights and welfare of the individual human subject.

These values have been the object of public discourse for at least the last 40 years. From the enunciation of the Nuremberg Code by U.S. judges in 1946, to the latest redraft of NIH and FDA regulations on human experimentation in response to congressional mandate in 1981; to these congressional hearings.

It is the obligation of Congress to define the boundary of legitimate human experimentation in this country, and of the FDA and NIH and other agencies to see to it that these boundaries are respected. It is my social role, and that of others concerned with human rights in health care, to advocate the rights and welfare of the potential subjects of human experimentation.

Let me address permanent implants first, and then turn my attention to temporary.

I believe the permanent artificial implants should be suspended because of the devastating results they have had on subjects and their families, and because their original justifications are no longer valid, and because the consent process is too primitive to protect the rights and welfare of human subjects.

For an experiment to be legally and ethically acceptable, it must be reasonable, based on scientific knowledge and a weighing of the benefit ratio; and thereafter, the subject must be given his or her informed, voluntary, competent and understanding consent.

Neither of these independent conditions is any longer satisfied by experimentation with the Jarvik-7 as a permanent device.

An article of the Nuremberg Code states unequivocally: "No experiment should be conducted where there is *a priori* reason to believe that death or disabling injury will occur."

It is possible to make an argument that the initial implant of Barney Clark was justifiable, in that there was no known *a priori* reason that it would cause such devastating results. But I believe it is no longer possible reasonably to make this argument.

The recipients have died and/or have suffered devastating and disabling strokes and experienced serious bleeding problems. There is simply not enough known about the blood-material incompatibility and anticoagulation therapy to prevent either bleeding or strokes, for this device to be used in humans on a permanent basis at this time. I believe more animal and laboratory research is required before human experimentation can ethically recommence.

Two primary justifications are nonetheless offered as arguments to continue experimentation with the Jarvik-7 as a permanent implant:

The patients are dying so there is nothing to lose; and as long as the adult patient consents, he should not be deprived of a possible benefit.

Neither argument, I believe, justifies continuation of the experiment.

First, dying patients need protection. Both the FDA and the U.S. Supreme Court have recognized this by insisting that the protection of the food, drug, and cosmetic laws apply to the terminally ill.

The Supreme Court has stated unequivocally, and I quote:

> For the terminally ill, as for anyone else, a drug is unsafe if its potential for inflicting death or physical injury is not offset by the possibility of therapeutic benefit.

Second, article 1 of the Nuremberg Code, and the FDA and NIH regulations make clear, that while informed consent is a necessary precondition to acceptable human experimentation, it alone is not sufficient.

The existence of the FDA itself, is, of course, based on the premise that the consent of the public to quackery and unapproved drugs and medical devices is insufficient justification to permit their marketing, or even to make them available, even to dying patients.

Moreover, informed consent alone cannot justify this experiment. But informed consent is necessary.

And in this regard it should be pointed out that there are major problems with Utah's consent form, used for the Barney Clark implant, and there remain, I believe, a series of crucial, protocol, and consent process issues, which are unresolved at Humana, and that individually and collectively demand resolution before obtaining an informed consent of a potential candidate would even be possible.

These can be outlined briefly:

No. 1, the assertion in the protocol that the primary goal is therapy cannot stand scrutiny.

No. 2, none of the experimental studies so clearly described in the protocol are detailed at all in the current consent form.

No. 3, there is no discussion of a plan for how the patient will die, and how the decision to terminate the experiment will be made.

No. 4, there is no provision made for decisionmaking regarding the experiment after the patient becomes incompetent, or is otherwise unable to communicate his desires to his family in the experiment.

No. 5, the Humana publicity clause, I believe, is unprecedented and unacceptable.

No. 6, as Mr. Schroeder pointed out, I believe much more serious attention needs to be devoted to the role of the patients' spouse and family members. It has become evident that in a large measure permanent artificial heart implantation is a family affair.

No. 7, the Humana Institutional Review Board, the IRB, seems especially unable to come to grips with any of these issues.

What is probably unfair, on the other hand, is to single out Humana IRB for its shortcomings in reviewing the protocol, and designing the consent form and process for permanent artificial heart implantation.

As Professor Al Jonsen has observed about the Utah IRB and their work on the Barney Clark consent form and process, quote:

> It was like asking them to design a Boeing 747 with Wright Brothers parts.

No local IRB, I believe, can be expected to do anything but a poor to miserable job of reviewing an artificial heart protocol and designing a consent process for it.

Indeed, local IRBs, originally thought of as adding an extra layer of protection for the subjects of human experiments, may have become more a part of the problem than the solution. At least in the cases of the artificial heart and xenograft research, they have tended to be viewed as procedurally legitimizing experimentation that is extremely difficult, if not impossible, to accept on the basis of substantive guidelines, like the Nuremberg Code, and the Federal regulations.

I believe both the Humana IRB and the FDA need to address this question: If the devastating results to the subjects of the first four artificial heart implants aren't sufficiently disabling to warrant suspension of further experimentation of the Jarvik-7 as a permanent implant, what consequences to subjects would warrant such a suspension or moratorium?

Now I would like to bring my attention to an issue, I believe, is more important. Because while temporary artificial hearts seem more benign, I believe that temporary artificial heart implants should also be suspended until we develop uniform and equitable patient selection criteria; a uniform protocol and consent process; and an acceptable national priority system for human heart transplantation.

Regulation of temporary heart implants has more urgency than that of permanent implants for a number of reasons:

First, there has been a *de facto* moratorium on permanent artificial implants.

Second, The FDA has agreed on the need to review each additional implant separately.

Third, Dr. William DeVries has been working on and thinking about both the technical and ethical issues in artificial heart implantation for more than 5 years, and has demonstrated that he is sensitive to the issues and open to suggestions to improve both the technical and ethical aspects of the procedure.

On the other hand, temporary implants have consistently been justified by their implanters on untenable grounds; have no master scientific protocol; have no standard consent protocol or patient selection criteria; and utilize wildly varying consent forms and consent processes.

The situation with temporary use in this country is almost completely out of control. And the real possibility exists that the tragic "me too" orgy of heart transplants that followed Dr. Christian Barnard's first human heart transplant in 1968 could be repeated.

It was absolutely remarkable to me that Dr. Jarvik used comparison for the 50 first artificial hearts, with the first 50 human heart transplants done in the world; literature, which is uniformally viewed as the blackest mark in the history of cardiac surgery, and probably in the history of surgery. No one wants to repeat, I hope, that. In that experiment we had 60 groups around the world, doing 100 transplants in a year, and all of them—except Dr. Shumway's group—then stopping because the results were so horrible.

That is precisely the kind of thing I think FDA should be designed to preclude. But I believe, as you pointed out, Mr. Chairman, the first problem with temporary use that deserves to be underlined is that there can be no reasonable certainty that planned temporary artificial hearts will not turn out to be permanent.

This can happen if a suitable heart donor cannot be found, but much more likely if the recipient suffers severe complications, such as stroke or kidney failure, that makes the recipient ineligible for a human heart transplant.

Accordingly, temporary artificial implants, since many of them will be permanent, should be at least as well thought out, planned for, and consented to, as permanent hearts. All the issues outlined regarding permanent artificial heart must be addressed by those contemplating use of the artificial heart as a temporary device.

FDA's current double standard, which applies very high standards to Dr. DeVries, and almost no standards to other people using the device as a temporary device, cannot, I believe, stand scrutiny and cannot be permitted to continue.

Two primary justifications, and we have heard them today, have been advanced for the use of the temporary artificial heart:

First, the patient was dying; and second, it was an emergency.

I have already discussed the issue of the dying patient, in that they deserve the same protection as everyone else.

As to the emergency nature, use of this justification in this context, I believe, is misplaced. The rejection of the human heart or the inability to locate a human heart donor are emergencies in the sense that the patient will likely die if something is not done. But they are not emergencies in the sense that they are not anticipated. Rejection is a known complication of heart transplantation, and with the continuing shortage of human hearts it is also known that a certain percentage of individuals will die on the waiting list.

In short, the use of the term "emergency," is an excuse, not a valid reason for unplanned human experimentation with temporary devices.

Third, informed consent forms and processes devised by the first four centers to use the artificial heart as a planned temporary measure are all different, and all signficantly inadequate.

I have not seen Houston's form, so I assume that is probably different, too, but I don't know the answer to that.

And they suffer from all or almost all of the shortcomings involved in obtaining informed consent for permanent use.

I believe informed consent must be taken seriously enough that there are uniform minimal standards that all centers using temporary artificial hearts should meet regarding informed consent. Of course, these should be developed in conjunction with the uniform master protocol so that some useful scientific information can be obtained from all the centers' use of this device.

The current consent form and processes for the four centers at which six temporary implants have taken place, demonstrate major variations on significant issues that must be clarified and agreed before further implants are permitted.

Just to outline those differences and divergencies:

No. 1, the description and the nature of the experiment as contrasted with the artificial heart's past use.

No. 2, the description of the risk/benefit ratio.

No. 3, the ability to withdraw from the experiment and a manner that the patient is likely to die.

No. 4, proxy consent.

No. 5, waivers.

And No. 6, what will happen to the patient if a human heart transplant is not performed.

All of these, as well as the issues of payment for the device and the procedure, are both important enough and common enough to be dealt with in a uniform manner.

It now seems apparent that neither the manufacturer nor the hospital will voluntarily form a multicenter review panel to develop uniform standards related to the protocol, patient selection criteria, and minimum standards for informed consent, and process.

No planned temporary artificial heart implant should be performed until an acceptable national system of allocating human hearts among individuals on the waiting list is agreed upon and in place.

And this point is important, because as long as there is a shortage of human hearts for transplantation, use of temporary artificial hearts cannot save lives. They cannot save lives because the total number of heart transplants that can be done in this country is limited by the total number of transplantable human hearts available.

Use of temporary artificial hearts can only change the identity of those who receive heart transplants. As long as there is a shortage of human hearts it can reasonably be argued that even if the technical and consent problems can be resolved, temporary artificial hearts should not be implanted because they are useless to the health care system as a whole—since they save no net lives—are extremely expensive, and add significantly to already high costs of heart transplantation.

I actually personally believe that. Even if I did not, I would oppose use of temporary artificial hearts until an equitable and agreed upon method to allocate human hearts was developed. Because otherwise, use of these devices changes the identity of who will receive the limited number of human hearts in a way that is intrinsically unfair.

It does this because surgeons are currently able to put patients who have temporary artificial hearts in front of the line for the next available human heart—giving them priority over other individuals who may have been on the waiting list longer, may be better suited for the available heart, may be in better physical condition to benefit from the available heart, and so forth, and who may well die because of this unfair reallocation.

So, let me conclude then, by noting that permanent artificial hearts did not create, of course, all the problems that they have exposed in our informed consent procedures and IRB review procedures, and obviously, temporary artificial hearts did not create the problems they have exposed in the allocation of human hearts for transplant.

Nonetheless, these problems are real, and the advent of the artificial heart provides us with an opportunity to take meaningful action that will not only protect potential recipients of the artificial heart, but will also help set high standards for other controversial human experiments, and develop fair and equitable allocation schemes for human organs.

To this end, I believe Congress should enact legislation to require the FDA and NIH to establish a joint review and oversight committee made up primarily of nonphysicians and nonscientists, to review the protocols, patient selection criteria, and informed consent forms and procedures for artificial heart implants, both permanent and temporary, xenografts, human embryo research, genetic engineering, and any other human experiment referred to it by NIH or FDA, and to monitor these experiments.

Enabling legislation should require that this review committee conduct all of its business in public and that all information made available to the committee be available to the public as well. Human experimentation is a public enterprise, and the use to which humans get put as well as the mandatory minimum procedures used to protect their rights and welfare are matters of serious public concern.

I believe we are not taking these issues seriously enough today and it is imperative that we reassert the importance of human values implicit in the Nuremberg Code, before it is quietly rewritten by well-meaning inventors and researchers.

Thank you very much, Mr. Chairman.

[The prepared statement of Dr. George J. Annas follows:]

TESTIMONY

presented before the

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

of the

COMMITTEE ON SCIENCE AND TECHNOLOGY

UNITED STATES HOUSE OF REPRESENTATIVES

on

Legal and Ethical Issues in Artificial Heart Experimentation

on

February 5, 1986

by

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LEGAL AND ETHICAL ISSUES IN ARTIFICIAL HEART EXPERIMENTATION

Mr. Chairman and members of the Subcommittee, thank you for inviting me to address the legal and ethical issues involved in artificial heart experimentation. Artificial heart implants represent the most public human experiments in the history of the world, and the manner in which they are conducted is a matter of utmost public concern since it graphically portrays the seriousness with which we take our laws and ethical rules regarding the protection of the rights and welfare of human subjects. Legal and ethical standards of human experimentation have long been a primary interest of mine. I was a consultant to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research established by Congress in 1974, have written a book on the Rights of Hospital Patients (1975), and co-authored a volume on Informed Consent to Human Experimentation (1977). More recently my work has focused in the area of transplantation and implantation of human and mechanical organs. From 1983 to 1985 I was chairman of the Massachusetts Task Force on Organ Transplantation, and over the past three years I have written a series of short articles on artificial heart experimentation which are appended to this testimony. I also serve as chairman of the Legal Advisers Committee of Concern for Dying, and chairman of the American Bar Association's Committee on Legal Problems in Medical Practice (Science and Technology Section). My testimony today represents my own views, and does not necessarily reflect the positions of any of these groups or organizations.

My general view is that ethics and law have taken a distinctly back seat to notions of scientific advance; that artificial implant experimentation is being conducted almost in an historic vacuum with scant regard for existing norms and codes of human experimentation; that NIH and FDA have been unable or unwilling to supervise or control implant experimentation; and that therefore additional steps must be taken to safeguard the rights and welfare of human subjects of future implant experimentation.

Before I outline the reasons for these disturbing conclusions, let me emphasize that I don't question the motives of any of the players in this drama. Indeed, in the arena of human experimentation, all involved have different and appropriate social roles. It is Dr. Robert Jarvik's social role to improve on the artificial heart; It is Dr. William DeVries' social role to attempt to use the artificial heart to benefit his patients; It is Dr. Jack Copeland's social role to try to save his patients' lives in extreme situations. But the roles of inventors, researchers, and surgeons do not exhaust the universe. In dealing with human experimentation, we are dealing with an area that we have come to recognize involves public values which are crystalized in our view of the rights and welfare of the individual human subject. These values have been the subject of public discourse for at least the last forty years; from the enunciation of the Nuremberg Code by U.S. judges in 1946, to the latest redraft of NIH and

FDA regulations on human experimentation in response to Congressional mandate in 1981, to these Congressional hearings. It is the obligation of the Congress to define the boundaries of legitimate human experimentation in this country, and of the FDA and NIH and other agencies to see that these boundaries are respected. It is my social role, and that of others concerned with human rights in health care, to advocate for the rights and welfare of the potential subjects of human experimentation.

Because the rights and welfare of potential subjects of experimental artificial heart implantation are not being adequately protected, I strongly believe there should be a moratorium on all such implants until their scientific reasonableness, proper use, clear patient selection criteria, adequate informed consent procedures, and clear rules on stopping individual experiments have been developed and approved by a joint review and oversight committee of the FDA and NIH. Permanent artificial heart implants should be at least temporarily suspended because of the devastating results they have had on subjects and their families, because their original justifications are no longer valid, and because the consent process used is too primitive to protect human subjects. Temporary artificial heart implants should be suspended for the same reasons, and additionally because the United States has yet to develop a fair and equitable method for allocating scarce human hearts. Let me first deal with permanent implants, and then address the somewhat more complicated issue of "temporary" use of implants.

I. Permanent artificial implants should be suspended because of the devastating results they have had on subjects and their families, because their original justifications are no longer valid, and because the consent process is too primitive to protect the rights and welfare of human subjects.

Acceptable human experimentation must be conducted in accordance with the principles of the Nuremberg Code and federal regulations governing human experimentation. For an experiment to be legally and ethically acceptable, it must be reasonable, based on scientific knowledge and a weighing of the risk/benefit ratio; and thereafter the subject must give his or her informed, voluntary, competent and understanding consent. Neither of these independent conditions is any longer satisfied by experimentation with the Jarvik-7 as a permanent device.

(a) Permanent Implantation of the Jarvik-7 can no longer be considered a reasonable medical experiment

Article 5 of the Nuremberg Code states that "No experiment should be conducted where there is a priori reason to believe that death or disabling injury will occur; except perhaps in those experiments where the experimental physicians also serve as subjects." Obviously this is not one of those "exceptional" experiments. The question thus is, is there "a priori reason to believe that death or disabling injury will occur" as a result of the experiment? This question can only be answered by examining the record of the experiment to date. Prior to the first implant, in

Dr. Barney Clark, the researchers believed that their patient would either die on the operating table, or go home within about 10 days.[1] The catastrophic disabling condition that required hospitalization for the rest of his life (112 days) was completely unanticipated and unplanned for. Dr. William DeVries has since done three additional implants. After his second implant patient suffered a stroke, Dr. DeVries is quoted as having said:

> "...it's impractical on the basis of two patients to determine whether or not these questions [whether society can afford artificial heart implants] can be answered. The third patient may have a stroke, the fourth patient may have a stroke, the fifth patient may have a stroke. In that case, the question is not going to be can society pay for it. The question will be: is it proper to even do this? Should it even be done anymore?"[2]

And after the first four permanent artificial heart implants, the director of the Humana Heart Institute was asked how Humana could argue that any progress was being made given the severe problems suffered by the recipients. Dr. Lansing replied: "Yes, there is progress. [William] Schroeder is improving and showing signs of recovery; [Murray] Haydon will soon be off the respirator and beginning to make a recovery; and yes, [Jack] Burcham has required dialysis for a pre-op condition, but we hope it is temporary. All the patients are living, and at this time none of the three has a condition that is either irreversible or immediately life-threatening."[3] This statement, made on April 24, 1985, unfortunately turned out to be wishful thinking. Within hours, Mr. Burcham was dead. Mr. Schroeder has suffered subsequent devastating strokes, and Mr. Haydon has not been able to leave his intensive care room for more than brief periods. The only other patient in the world to receive the Jarvik-7 as a permanent implant, Leif Stenberg, suffered a stroke and died, and the Swedish surgeon who did the implant, Bjarne Semb, has said publicly that he will not do any more implants because the device is simply too crude and causes such terrible effects in its recipients. Of Mr. Stenberg, Dr. Semb said, "He might as well have died."[4]

It is possible to make an argument that the initial implant in Barney Clark was justifiable in that it was not known "a priori" that it would cause such devastating results. It is no longer possible reasonably to make this argument. Recipients have died and/or suffered devastating and disabling strokes or seizures, and experienced serious bleeding problems. There is simply not enough known about anticoagulation therapy to prevent either bleeding or strokes for this device to be used in humans at this time. More animal and laboratory research is required before human experimentation can ethically recommence.

It should also be underlined that while the inventor and researcher may believe in the Jarvik-7, almost no one else does. The NIH Working Group, for example, while endorsing research on fully implantable electrical artificial hearts, noted that "pneumatically actuated...systems that do not permit substantial levels of ambulation and relatively normal activity are importantly suboptimal."[5] It also noted that "None of the [pneumatic] devices had proven durability in animals according to a rigorous formal protocol."[6]

Two primary justifications are nonetheless offered as arguments to continue experimentation with the Jarvik-7 as a permanent implant: the patients are dying, so there is nothing to lose; and as long as the adult patient consents, he should not be deprived of a possible benefit. Neither argument justifies continuation of the experiment.

(i) Dying patients deserve protection

The law has recognized that certain populations are especially vulnerable to exploitation in the human experimentation arena, and special protections have been devised for children, prisoners, and mental patients.[7] But perhaps the most vulnerable population of all is that comprised of the terminally ill. The FDA and the United States Supreme Court have recognized this by insisting that the protection of the Food, Drug and Cosmetic laws apply to the terminally ill. The court has stated unequivocally, "For the terminally ill, as for anyone else, a drug is unsafe if its potential for inflicting death or physical injury is not offset by the possibility of therapeutic benefit." And later in the same opinion, "To accept the proposition that the Food, Drug and Cosmetic Act has no relevance for terminal patients is to deny the Commissioners' authority over all drugs, however toxic or ineffectual, for such individuals...the terminally ill no less than other patients [deserve protection] from the vast range of self-styled panaceas that inventive minds can devise."[8] The worldwide "death with dignity" movement and the right to refuse treatment movement likewise insist that we honor the liberty interests of the terminally ill. Terminal illness alone can never be a justification for doing experiments on human beings.

There are many reasons for this. First, the terminally ill retain all their rights as citizens until their death, and deserve full protection of the law. Second, although we may know that they are dying, there is no scientific way to tell exactly when they will die.[9] Third, the terminally ill are especially vulnerable to manipulation and exploitation and the notion that anything can be done that "saves a patient's life" embodies what Yale Law School psychiatrist Jay Katz has described as the "magical myth": that the physician actually has the power to conquer death. As he has noted, "at such times all kinds of senseless interventions are tried..."[10] Fourth, related to this, as Harvard Medical School surgeon, Dr. Francis Moore, has noted, this type of innovation will actively be sought by "desperate patients" who want to be subjects, and the procedure will be seen by them as their only "hope for survival".[11] Fifth, the choice is not between life or death. As history has illustrated, the choice is between two different ways of dying. Under Congressional mandate, NIH has devised special regulations and protections for prisoners, children, fetuses and mental patients. It may be time to devise special procedures to protect the terminally ill as well.

(ii) Informed consent is a necessary but not sufficient precondition for acceptable human experimentation

As Article One of the Nuremberg Code, and the FDA and NIH regulations make clear, informed consent is a necessary precondition to acceptable human experimentation, but it alone is not sufficient. The existence of the FDA itself is based on the premise that the consent of the public to quackery and unapproved drugs and medical devices is not sufficient justification to permit their marketing. The point is that we do not permit certain items even to be offered to patients because we *know* they will accept them since they are in no position to be able to refuse them. Laetrile is one famous example. Dying cancer patients are often desperate, and desperate individuals will often "consent" to treatments that are dangerous and/or ineffective. This raises two issues. The first is that *certain things should simply not be offered to desperate patients* even if they will accept them, because all the evidence we have indicates that they are dangerous and cannot help the patient. A patient agreeing to have his heart removed and replaced by a mechanical device that is dependent upon a 300 pound drive cart may be the most extreme example of this. But there are others. We would surely not permit researchers working on a cure for AIDS to do *anything* to AIDS patients that these patients consented to. We would want the protocols carefully reviewed, the risk/benefit ratio worked out, and a solid scientific basis for the experiment articulated. Even then, if the experiment presented an *a priori* likelihood of death or serious disability, we would not (or at least should not) permit it even though we could recruit subjects for it.

Dr. William DeVries asserted prior to the Barney Clark implant, "Many people have asked us the question as to - it's not fully implantable, why then would you do it? Why don't you wait ten years, when its implantable, and then do it. *But the key is informed consent*. Why should I let people die, when I can give them a chance to live - if they're willing to accept the limitations of the external pumping system?"[12] The implication is that informed consent alone justifies the experiment and this is incorrect. Indeed, it perverts the very essence of informed consent, converting a doctrine designed to be a shield for patients from procedures they don't understand or want, into a sword to justify doing things to them that otherwise would be unacceptable to do. But the subject's "informed consent" does not make an otherwise unacceptable procedure acceptable. Dr. DeVries simply begs the relevant question: how can we determine when it is reasonable to offer a permanent artificial heart to a human being?

On the other hand, Dr. DeVries is certainly correct to insist that informed consent is a necessary prerequisite to acceptable human experimentation; and if it cannot be obtained, the experiment cannot be lawfully or ethically performed. In this regard, the current consent process at Humana Audubon is far too primitive to give a neutral observer any confidence that informed consent is actually being obtained. On this we have first Dr. DeVries' own assessment, made in May, 1985, after performing his four implants. Dr. Lawrence K. Altman reports that "Dr. DeVries has repeatedly said that the four men in whom he has implanted artificial hearts were so coerced by their disease that they felt that death was their only alternative. In signing the 17-page informed consent forms, each recipient, Dr. DeVries has said, 'told me in their own way that they didn't care' if they read it or not, and had signed it primarily because they had to get the device."[13]

Dr. DeVries here raises the question as to whether we can ever justify experimentation on very sick, terminally ill patients. The answer is that we can only justify experimentation on such individuals, individuals who we know *a priori* are severely coerced by their diseases, if we provide them with *more protection than we would healthy volunteers.* One thing we cannot justify in this group of patients is to put the burden on them to decide if the research project itself is scientifically reasonable and if the risk/benefit ratio is socially acceptable. By refusing to resolve this issue itself, and by putting the burden of its resolution on Dr. Clark, the Utah IRB abdicated its responsibility to determine if implanting an artificial heart in a human being that required lifetime tethering to a clumsy drive cart was acceptable.

But this is just the beginning. There were major problems with Utah's consent form used for Barney Clark (see Appendix I), and there remain a *series of crucial protocol and consent process issues* that are unresolved at Humana and that individually and collectively demand resolution before obtaining the informed consent of a potential candidate will even be possible. These can be briefly outlined:

1. The assertion in the protocol that the primary goal is therapy cannot stand scrutiny. It has confused both members of the IRB and patients, and must accordingly be changed.

2. None of the experimental studies so clearly described in the protocol are detailed at all in the consent form (including invasive studies like the hemodynamics studies; the studies with the Heimes driver; and the pharmocological studies, including Isoproterenol, Dopamine, Sodium Nitroprusside, Nitroglycerin and Ephedrine). This must be corrected.

3. The "right to withdraw clause" has been omitted, and there is no discussion of or plan for how the patient will die and how the decision to terminate the experiment will be made. If the patient is competent, the patient has a legal right to discontinue the experiment and this must be explicitly preserved, and provisions made for its exercise. Without this clause death may seem to be escapable and denied by all concerned.

4. No provision is made for decisionmaking regarding the experiment after the patient becomes incompetent or otherwise unable to communicate his desires to the experimenter. Provision for prior appointment of a proxy by the patient should be part of the standard consent procedure.

5. The Humana publicity clause is unprecedented and unacceptable.[14] Subjects have never before in the history of human experimentation been required to sign away all rights to privacy regarding every mode of public communication regarding their case. This clause should be deleted and a fairer confidentiality statement substituted for it.

6. Much more serious attention needs to be devoted to the role of the patient's spouse and family members. It has become evident that in a large measure permanent artificial heart implantation is a family affair. Indeed, the spouses of the patients have so far devoted all or much of their entire lives to caring for their husbands while they are alive, and to discussing and explaining the experience. The notion that some of the recipients had that they wanted to make the decision on their own and not "burden" their spouse and family members turned out to be a fantasy. The Humana protocol requires the patient to have a supportive family; the

family's role in the consent process and in followup care and termination of the experiment needs to be highlighted and articulated. Spouses should have clear veto power over the experiment and subjects should understand the severe burden this experiment will put on their family.

7. The Humana Institutional Review Board (IRB) seems especially unable to come to grips with any of these issues. In my own discussion with members of the Humana Audubon IRB in August, 1985, for example, members vigorously defended such propositions as: (1) the implant procedure is not experimental at all, but "the whole thing is therapeutic"; (2) informed consent is "just a parade of horribles" that serves only to scare patients; and (3) withdrawal from the experiment by the research subject would be "murder" if the researcher permitted it and turned off the artificial heart.

On the other hand, it is probably unfair to single out the Humana IRB for its shortcomings in reviewing a protocol and designing a consent form and process for permanent artificial heart implantation. As Professor Albert Jonsen has observed about the Utah IRB and their work on the Barney Clark consent form and process, "It was like asking them to design a Boeing 747 with Wright Brothers parts." No local IRB can be expected to do anything but a poor to miserable job of reviewing an artificial heart protocol and designing a consent process for it.

IRBs, originally thought of as adding an extra layer of protection for the subjects of human experiments, may have become more a part of the problem than the solution. At least in the cases of artificial heart and xenograft research, they have tended to be viewed as procedurally legitimizing experimentation that is extremely difficult, if not impossible, to accept on the basis of substantive guidelines, like the Nuremberg Code and the federal regulations. In fact, they are often much more true to their name than their intended function: protecting their institution from outside criticism as a first priority, and only worrying about protecting the patient if this protection seems consistent with the interests of the institution.

Accordingly, Congress should consider legislation to require FDA and NIH to establish a joint national review and oversight panel composed primarily of non-physicians and non-scientists to review and monitor protocols, patient selection criteria, and design consent forms and processes for highly controversial and complex human experiments, including artificial heart implantation (permanent and temporary), xenografts, human embryo research, genetic engineering, and any other contemplated human experiment deemed to warrant such review by FDA or NIH. In conducting such review and monitoring, all information made available to the review committee should be public information, and their deliberations should be public as well.

In the meantime, FDA should be specifically requested to respond to the following question: If the devastating results to the subjects of the first four artificial heart implants aren't sufficiently disabling and debilitating to warrant suspension of further experimentation with the Jarvik-7 as a permanent implant, what consequences to subjects would warrant such a suspension or moratorium?

II. Temporary artificial heart implants should be suspended until we develop uniform and equitable patient selection criteria; a uniform protocol and consent process; and an acceptable national priority system for human heart transplantation

Regulation of temporary heart implants has more urgency than that of permanent implants for a number of reasons. First, there has been a *de facto* moratorium on permanent artificial implants for almost a year because of the inability of Humana to locate another candidate in that time period. Much of this can be explained by the fact that all four of the recipients of permanent artificial hearts would *today* be candidates for human heart transplantation under the current patient selection criteria which has expanded rapidly in many centers over the past 12 months. Second, FDA has agreed on the need to review each additional implant separately and retains the ability to terminate the projected "series of seven" implants at any time it deems this action warranted. Third, Dr. William DeVries has been working on and thinking about both the technical and the ethical issues in artificial heart implantation for more than five years, and has demonstrated that he is sensitive to the issues and open to suggestions to improve both the technical and ethical aspects of the procedure.

On the other hand, temporary implants have consistently been justified by their implanters on untenable grounds, have no master scientific protocol, have no standard consent protocol or patient selection criteria, and utilize wildly varying consent forms and consent processes. The situation with temporary use in this country is almost completely out of control and a real possibility exists that the tragic "me to" orgy of heart transplants that followed Christian Barnard's human heart transplantation in 1968 could be repeated.

As the number of heart transplant centers grows, patient selection criteria will become much less strict, and the numbers of waiting candidates for human hearts will increase. Since the number of human hearts is not likely to increase substantially, more and more individuals will die on the waiting list. This has encouraged experimentation with "temporary" artificial hearts, but shouldn't permit us to ignore all of the ethical and legal constraints that help define acceptable human experimentation.

The first problem with "temporary use" that deserves to be underlined is that there can be no reasonable certainty that the planned "temporary" artificial heart will not turn out to be permanent. This can happen either if a suitable heart donor cannot be found, or, much more likely, if the recipient suffers a severe complication (such as stroke or kidney failure) that makes the recipient ineligible for a human heart transplant. Accordingly, temporary artificial implants should be at least as well thought out, planned for, and consented to as permanent artificial hearts, and all of the issues outlined regarding permanent artificial hearts must be addressed by those contemplating use of the artificial heart as a temporary device.

(a) The justifications for performing experiments with temporary implants without proper FDA, IRB or other review, and without adequate informed consent procedures are not persuasive

As of this hearing, there have been seven planned temporary implants using four different devices. The first two implants were performed by Dr. Denton Cooley in 1969[15] and 1981.[16] (See Appendix II) Dr. Cooley had neither of these implants reviewed or approved by the FDA, an IRB, or any other review method. He argued that they were both therapeutic and not experimental, and were done in emergency conditions to save the patient's life. Both patients died shortly after receiving a human heart transplant. No further temporary implants were attempted until March, 1985, when Dr. Jack Copeland inserted an artificial heart, developed by a dentist for use in animal experimentation, into the chest of Thomas Creighton. He also died shortly after receiving a human heart transplant. (See Appendix III) This implant occassioned a public debate about the role of the FDA in such experimentation, and the FDA has since taken a stance that it will not attempt to regulate individual "emergency" uses of such experimental devices. Since then Jarvik-7 artificial hearts have been used as temporary devices in three patients at three different centers. In addition, in a separate and more carefully conducted study, another device, called the "Penn. State" heart, which was approved by the

FDA for temporary use, has been used once by Dr. William Pierce. His patient died 18 days after a human heart transplant. Of the Jarvik-7 implants, two patients remain alive after human heart transplant (See Appendix IV) and in one, at Abbott-Northwestern, the device threatens to be permanent.

In most of these cases, two primary justifications have been advanced for use of a temporary artificial heart: the patient was dying; and it was an emergency. Neither justification is sufficient to justify use of an experimental device of this nature in an unconsenting patient.

The arguments relating to dying patients are set out above with regard to permanent artificial hearts, and apply equally here. As to the "emergency" nature, use of this justification in this context is misplaced. Rejection of a human heart, or inability to locate a human heart donor, are emergencies in the sense that the patient will likely die if something is not done. But they are not emergencies in the sense that they were not anticipated. Rejection is a known complication of heart transplantation; and with the continuing shortage of human hearts, it is also known that a certain percentage of individuals will die on the waiting list. In short, use of the term "emergency" is an excuse, not a valid reason for unplanned human experimentation with temporary devices. Accordingly, no such device should be used without prior FDA review and approval, and without the informed consent of the patient. If use of a temporary device is contemplated, all human heart transplant patients should, at a minimum, be asked initially if they would consent to its use.

(b) The informed consent forms and processes devised by the first four centers to use the artificial heart as a planned temporary measure are all different and all significantly inadequate, and suffer from all or almost all of the shortcomings involved in obtaining consent for permanent use

Since the primary arguments given for use of the temporary artificial heart have involved its alleged "emergency" nature, the consent process has not been taken very seriously. Indeed, in at least two of the last five implants, the patients themselves did not participate in any meaningful way in the consent process. This should be unacceptable. No patient who does not personally consent to its implantation should be seen as an appropriate subject for experimentation with the artificial heart since this is such a profoundly radical experiment that can have such devastating effects on the subject.

Informed consent must be taken seriously, at least seriously enough that there are uniform minimal standards that all centers using "temporary" artificial hearts should meet regarding informed consent. Of course, these should be developed in conjunction with a uniform master protocol so that some useful scientific information can be obtained from multicenter use. The current consent forms and processes from the four centers, at which the last five temporary implants took place, demonstrate major variations on significant issues that should be clarified and agreed upon before further implants are permitted. Three of the four centers used the Jarvik-7 (in one case a smaller version), and the other a substantially similar device. The specific areas of disagreement or significant divergence include:

1. The description of the nature of the experiment as contrasted with the artificial heart's past use. One consent form, for example, describes it as having been "successfully implanted in five patients"; one says it "has supported life in growing calves for up to 260 days"; another that it has been subject to "extensive testing in experimental laboratory animals and humans"; and the fourth is silent on its past uses and results.

2. The description of the risk/benefit ratio. None mention two of the complications that all four of Dr. DeVries' patients have suffered: hemolytic anemia and immunosuppression; and only one mentions pulmonary insufficiency as a possible complication. One form says that all reasonable alternatives have been discussed, the other three allege that use of the artificial heart is the "only alternative" available to maintain life. But even among these three there are variations, one hedges with the phrase that it is "quite unlikely" that I will survive long enough to obtain a heart transplant without it, while another asserts there isn't "any possibility" of survival without use of the device.

3. The ability to withdraw. One form doesn't mention this issue at all; two others use boiler plate language common to most consent forms involving drug studies, and one uses somewhat reasonable language on the right to withdraw, "recognizing that such a decision after the total artificial heart is implanted will result in my death."

4. Proxy consent. None of the forms provide any mechanism for proxy consent; and one actually attempts to do away with the consent requirement altogether by providing: "If I am too sick to be consulted, I authorize such procedures as are *in the professional judgment of the medical staff necessary* and desirable for my life, safety or comfort." (emphasis supplied)

5. Waivers. Two forms have no waivers and three guarantee that confidentiality will be respected. One form, however, adopts the unacceptable publicity language of the Humana form[14] (Abbott-Northwestern), and another uses boiler plate products liability waiver language: "I expressly understand that no warranties are made with respect to the implant and use of the temporary artificial heart, and all express or implied warranties are disclaimed, including without limitation any warranty or merchantability or warranty of fitness for a particular purpose."

6. If a human heart transplant is not done. Only one form discusses what will be done in this case, and says simply, "you will be supported by the artificial heart as long as possible."

All of these issues, as well as the issue of payment for the device and the procedure, are both important enough and common enough to be dealt with in a uniform manner. It now seems apparent that neither the manufacturer nor the hospitals will voluntarily form a multicenter review panel to develop uniform standards related to the protocol, uniform patient selection criteria, and minimal standards for informed consent forms and processes. Accordingly, Congress should direct NIH and FDA to establish a joint national review and oversight panel, made up primarily of non-physicians, non-scientists, to review the protocols, patient selection criteria, and consent forms and processes with the charge of developing uniform minimal standards and monitoring the actual experiments.

(c) No further temporary artificial implants should be performed until an acceptable national system of allocating human hearts among individuals on the waiting list is agreed upon and in place

As long as there is a shortage of human hearts for transplantation, use of temporary artificial hearts cannot save lives since the total number of heart transplants that can be done is limited by the total number of transplantable human hearts available. The use of temporary artificial hearts can only change the identity of those who will receive heart transplants. As long as there remains a shortage of human hearts, it can reasonably be argued that even if the technical and consent problems can be resolved, temporary artificial hearts should still not be implanted because they are useless to the health care system (since they save no net lives) and are extremely expensive, adding significantly to the already high cost of heart transplantation. I personally believe this; but even if I did not, I would still oppose use of the temporary artificial heart until an equitable and agreed-upon method to allocate human hearts is developed, because otherwise use of these devices changes the identity of those who will receive the limited number of hearts available in a way that is intrinsically unfair.

It does this because surgeons are currently able to put patients who have temporary artificial hearts in the front of the line for the next available human heart - giving them priority over other individuals who may have been on the waiting list longer, may be better suited for the available heart, may be in better physical condition to benefit from the available heart, etc., and who may well die because of this reallocation. Perhaps society will decide that this is a proper thing to do; but it certainly has not made this decision yet, and until it does, prioritizing hearts in this fashion is arbitrary and unfair to all the patients in the United States waiting for human hearts (See appendix V for a discussion of competing allocation schemes).

III. Conclusion

Permanent artificial hearts did not create all the problems they have exposed in our informed consent procedures and IRB review, and temporary artificial hearts did not create the problems they have exposed in the allocation of human hearts for transplant. Nonetheless, these problems are real, and the advent of the artificial heart provides us with an opportunity to take meaningful action that will not only protect potential recipients of the artificial heart, but will also help set high standards for other controversial human experiments, and develop fair and equitable allocation schemes for human organs.

To this end, Congress should enact legislation to require FDA and NIH to establish as joint review and oversight committee, made up primarily of non-physicians and non-scientists, to review the protocols, patient selection criteria, and informed consent forms and procedures for artificial heart implants (both permanent and temporary), xenografts, human embryo research, genetic engineering, and any other human experiment referred to it by NIH or FDA, and to monitor these experiments. The enabling legislation should require that this review committee conduct all of its business in public, and that all information made available to the committee be available to the public as well. Human experimentation is a public enterprise, and the uses to which humans are put, as well as the mandatory minimum procedures used to protect their rights and welfare, are matters of serious public concern. We are not taking these issues seriously enough today and it is imperative that we reassert the importance of human values implicit in the Nuremberg Code before it is quietly rewritten by well-meaning inventors and researchers.

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3. "Surgeon DeVries' dream: 'forgettable' heart implant", American Medical News, May 10, 1985, 1, 58 (emphasis supplied).

4. "Surgeons Disagree on Artificial Heart", Science, 230:786 (15 Nov. 1985).

5. Working Group on Mechanical Circulatory Support of the National Heart, Lung, and Blood Institute, Artificial Heart and Assist Devices: Directions, Needs, Costs, Societal and Ethical Issues (May, 1985) at 33 (emphasis supplied).

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7. Annas, G.J., Glantz, L.H., Katz, B.F., Informed Consent to Human Experimentation: The Subject's Dilemma, Ballinger, Cambridge, Ma, 1977.

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10. Katz, J., The Silent World of Doctor and Patient, N.Y., Free Press, 1984 at 151.

11. F. Moore in "Ethical Aspects of Experimentation with Human Subjects", Daedalus, Spring, 1969 at 509.

12. Artificial Heart, NOVA, Transcript, p. 3.

13. Altman, L.K., "The Ordeal of a 'Human Experiment'", N.Y. Times, May 14, 1985.

14. The text of the clause is: "I am fully aware of the considerable public interest anticipated in my story as a recipient of a Total Artificial Heart. I am also aware that Humana Hospital-Audubon has an obligation to disseminate medical information concerning my hospital course as deemed appropriate in the judgment of my physician. In addition to those materials identified in paragraph 13 [relating to professional, scientific and FDA use of information] Humana Hospital-Audubon, as approved by my physician, is authorized to make, or permit to be made, photographs, slides, films, video tapes, recordings or other means of recording and/or communicating hereinafter referred to as "material(s)" that may be used in newspaper, magazine articles, television, radio broadcasts, movies or any other media or means of dissemination. I consent to the use of my name, likeness, or voice for such purposes. I agree that Humana Hospital-Audubon or Humana Inc. will be the sole and exclusive owner of such materials, and I release the Humana Heart Institute, Humana Inc., Humana Hospital-Audubon, their officers, agents and employees from all claims of liability with respect to the showing, use or dissemination of such material(s). I understand that the materials which are made public, as described in this paragraph, will protect my modesty and be within generally accepted bounds of good taste." (Aug. 8, 1985 revision)

15. Annas, G.J. et al, supra. note 7, at 11-14.

16. Caplan, A., "The Artificial Heart", Hastings Center Report, Feb. 1982, at 22-24.

APPENDICES CONGRESSIONAL TESTIMONY

I. Annas, G.J., Consent to the Artificial Heart: The Lion and the Crocodiles, *Hastings Center Report*, April, 1983, 20-22.

Commentary on the Barney Clark consent form.

II. Annas, G.J., Glantz, L.H. & Katz, B.F., *Informed Consent to Human Experimentation: The Subject's Dilemma*, Ballinger Pub. Co., Cambridge, Mass., 1977, 12-17, and 21-22.

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III. Annas, G.J., The Phoenix Heart: What we have to Lose, *Hastings Center Report*, June, 1985, 15-16.

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Consent to the Artificial Heart: The Lion and the Crocodiles

by GEORGE J. ANNAS

When Dr. Christiaan Barnard performed the first human heart transplant in 1967, he did not obtain informed consent. He purposely led Louis Washkansky to believe that the procedure had an 80 percent chance of success, instead of telling him that the probability applied only to his surviving the operation. Dr. Barnard's justification: "He had not asked for odds or any details . . . he was at the end of the line. . . . For a dying man, it is not a difficult decision. . . . If a lion chases you to the bank of a river filled with crocodiles, you will leap into the water convinced you have a chance to swim to the other side. But you would never accept such odds if there were no lion" (*One Life*, Macmillan, New York, 1969, p. 348).

Dr. Denton Cooley expressed similar thoughts about the first recipient of a temporary artificial heart. He said of Haskell Karp, "He was a drowning man. A drowning man can't be too particular what he's going to use as a life preserver. It was a desperate thing and he knew it."

Similarly, after implanting the first permanent artificial heart in Barney Clark, Dr. William DeVries argued that Clark unquestionably made the right choice: "He was too old for a transplant, there were no drugs that would help; the only thing that he could look forward to was dying (*Newsweek*, Dec. 13, 1982, pp. 35-36).

Dr. Barnard made no pretext of obtaining informed consent. Dr. Cooley did have Haskell Karp sign a consent form regarding the possible temporary use of a "mechanical cardiac substitute" in the event the operation to reconstruct his left ventricle was unsuccessful. But it was only the incredible conclusion of two federal courts (applying Texas law) that this first-of-its-kind procedure was primarily therapeutic, not experimental, that helped him prevail in a lawsuit brought by Karp's widow for failure to obtain informed consent.

Clark's operation occurred more than thirteen years after Karp's. During this period there have been highly touted advances in institutional review boards (IRBs) and the required documentation of informed consent for experimental procedures. One would expect the informed consent procedures used in the Clark case [illegible] of a very high order. And so they [illegible] seemed in the press. Indeed, Morris Abram, chairman of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, has been quoted as saying that the informed consent procedures followed in the Clark case are "a perfect example of what we recommended. The patient was fully able to comprehend and give autonomous consent. And there seemed to be total revelation by the medical team of what it planned to do and the possible risks and effects" (*Medical World News*, Jan. 10, 1983, pp. 13-14).

Although the consent procedure used in the Barney Clark case was an improvement over the earlier ones, it can hardly be characterized as "perfect."

The Consent Form

The FDA has put a temporary hold on further implants because the early fracture of one of the valves was unexpected. However, the agency has not questioned the consent process itself and sees consent as an IRB responsibility.

Almost everyone knows that Barney Clark signed an "11-page" consent form. Unfortunately the form is more notable for its length than its content. It is incomplete, internally inconsistent, and confusing. Consent is a process and not a form, but the form should reflect the process and advance the knowledge and autonomy of the subject. The form's most crucial shortcoming is that it assumes Dr. Clark will either continue to be competent and able to consent to further treatment, or that he will die. It takes no account of a "halfway success": survival coupled with severe confusion, mental incompetence, or coma. Two clauses deal with the predictable and likely probability that additional surgical procedures will be done following the initial implant. Obviously, if the IRB believes consent means anything in this context, these additional procedures would require it as well. Accordingly, one clause states that repair or replacement of the device would not be done unless with "a new consent form signed by me." The next clause contemplates testing the functioning of the heart by certain procedures, and guarantees that "each of these new procedures will have a consent form which must be signed before they are performed."

A number of surgical procedures have actually been required since the implantation, both to repair the artificial heart and to treat related complications (such as nosebleed). The consent form Barney Clark signed clearly contemplated that only he would be allowed to decide whether such additional procedures would be done, and that he would agree by signing additional consent forms. In fact, Barney Clark did not sign any new consent forms for any of these surgical procedures. Hospital officials considered him mentally incompetent; they sought his wife's signature on all subsequent consent forms, although he did verbally assent to the procedures. Nor are the forms his wife signed the specific forms mentioned in the original consent document, but rather the hospital's routine consent form. Neither Dr. Barnard nor Dr. Cooley faced this halfway success problem, but it should have been faced in Utah. Who would Dr. Clark have wanted to make decisions for him? On what basis should such decisions be made? And when should the experiment be ended from Dr. Clark's perspective?

This lack is especially ironic in view of the form's withdrawal clause: "I understand I am free at any time to withdraw my consent to participate in this experimental

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project, recognizing that the exercise of such an option after the artificial heart is in place may result in my death." Surely Dr. Clark must be afforded this option. But just as surely someone else whom he designated should have been empowered to exercise it for him, applying the criteria he would have wanted to apply.

There are at least two approaches to this quandary: the "living will" and the durable power of attorney. In a living will, Dr. Clark could have specified the conditions under which, should he become incompetent, he would want the experiment terminated. For example, how long would he want to continue if he remained incompetent and hospitalized? What if he became comatose? What if he required kidney dialysis to survive? These are predictable questions only Dr. Clark should answer.

The durable power of attorney also would be of use, but arguably only if the same type of instructions accompanied it. This instrument permits the designation of a proxy to make decisions for the individual that is valid even if the individual becomes incompetent. Though no court has yet ruled that such authority gives the proxy the right to make medical decisions, it should be recognized for this purpose

Excerpts from the Consent Form

1.1 It is the judgment of physicians and others who have evaluated my diagnostic tests that, although no specific life span can be estimated, it is probable that I will die much sooner than most others of my age and that while alive I will continue to be severely restricted due to my [illegible] I further understand that there are no further medical therapies that will arrest the course of this deterioration of my heart. Replacement of my natural heart is the only treatment. While prolongation of life beyond that expected for my condition by use of a mechanical heart has not been proven in humans, nevertheless I am willing to submit to its implantation on an experimental basis in order to determine if it will help people with my condition. . . .

I hereby authorize Dr. William C. DeVries, who is referred to hereafter in this special consent as "my physician," and such assistants and associates as he may designate, to implant a mechanical artificial heart in place of my diseased natural heart. Any consideration as to my selection for a heart transplant procedure would be determined by an independent cardiac transplantation team from another medical center. I understand that if I do not meet their criteria for a future heart transplant, I must accept the artificial heart as a final life-sustaining device. It is most probable that the artificial heart will be a final life-sustaining device for an undefined period. . . .

2.1 I hereby request and authorize my physician to proceed with the implantation of an experimental total artificial heart device. I *recognize that the ventricles* (the larger two of the heart's four pumping chambers) *from my own natural heart will be removed* and a mechanical heart device will be placed within my chest in the space formerly occupied by my own natural heart, and that this mechanical device will require my body to be attached to an air-driving system by two plastic six-foot long air tubes to pump my blood through my mechanical heart and circulate it through my body. I am aware that my life style will be significantly different with an artificial heart. My activity will be *severely limited* because of the drive lines. The external drive systems will not necessarily require me to be bedridden but at best would allow me to move from room to room, and may allow brief periods of being outside and riding in a car or van if it is capable of carrying the external drive system. I may be able to carry on many life functions in a normal manner (e.g. toilet activity, eating, reading and desk work). It is possible, however, that I may have to remain bedridden due to pain, weakness or other problems. . . .

2.2 I further understand that due to the positioning and nature of the artificial heart if it is installed, that in addition to the surgery necessary for the original installation, additional chest surgeries may be required in the event the device needs to be replaced or repaired which will be explained to me and will be done with a new consent form signed by me for each such procedure and that in all likelihood, general anesthesia with its attendant risks would be necessary in connection with such procedures.

2.3 I also understand that if the artificial heart device is installed that I can anticipate considerable postoperative pain and discomfort similar to or greater than that which would be experienced following the usual type of cardiovascular surgery, and that additional or prolonged discomfort and pain may result in the event of further surgery. I also understand that the use of the artificial heart may necessitate additional instrumentation and studies in order that adequate information may be obtained concerning its functioning, and such instrumentation and studies are expected to consist of or be similar to those involved in cardiac catheterization but may include other procedures, with attendant risks, discomfort and inconvenience. Each of these new procedures will have a consent form which must be signed before they are performed. . . .

8. I acknowledge that my physician has in a satisfactory manner, explained to me the procedure involved in the implantation of the artificial heart into my body and that all questions that I have asked about the procedure and its attendant risks, including death, the experimental nature of the artificial heart, its expected function, the probable restrictive nature of my life following the procedure, the probability of continued hospitalization and medical care, have been answered in a manner satisfactory to me. . . .

provided such decisions are consistent with the prior expressed wishes of the person or the person's "best interests." Standing alone, however, with no indication of the person's actual desires concerning treatment, the durable power of attorney does not add much to our knowledge of Dr. Clark's own wishes.

It might be argued that no one knows what Dr. Clark would want done better than his wife (and this may be true), but unless Dr. Clark has made his wishes known to her and designated her as the person to carry them out, we can only speculate on this issue. Just as we would not have allowed Mrs. Clark to consent to the heart implant on behalf of her husband, we should not permit her to consent to its termination or to additional procedures related to it on his behalf.

The problem is one of ascertaining Dr. Clark's own wishes. His son, Dr. Stephen Clark, a surgeon, said on the day of the operation: "Even with his illness, he still maintained a great interest in life. If, however, he finds out that while he is alive he still has a lot of pain and a lot of nausea, he will be very disappointed. I don't think he would want that. . . . As long as he is comfortable, he has enough things in life to enjoy" (*New York Times*, Dec. 4, 1982, p. 14).

Other Problems

Other shortcomings in the form deserve at least passing mention, because they indicate a lack of attention to detail in the entire process. Though the form is entitled a "Special Consent for Artificial Heart Device Implantation and Related Procedures," the "artificial heart device" itself is variously designated "a mechanical heart," a "mechanical artificial heart," an "artificial heart," a "mechanical heart device," an "experimental total artificial heart device," and "the device." The clauses on alternatives are also ambiguous at best. One assures that "replacement of my natural heart is the only treatment"; another that "I have discussed alternative treatments with my physician [including drug treatment and surgical repair of my heart]."

Other clauses simply appear to have been cut and pasted from standard hospital consent forms:

> I consent to the administration of anesthesia as arranged by my physician with such assistants as may be designated, and to the use of such anesthetics as they may in their judgment deem advisable.
>
> I hereby authorize the University of Utah Hospital, through its authorized agents, to dispose of or use for any purpose, any tissue or body parts which may be removed during the surgical procedures.

The first adds nothing to the consent (unless we assume that Clark thought the procedure could be performed without anesthesia), and the second is so overbroad in this context as to be macabre. The only "tissue or body part" being removed are Dr. Clark's left and right ventricles, and requiring Clark to agree that they could be used "for any purpose" (display in an art museum or in the Smithsonian? sold to the *National Enquirer*?) is bizarre. This clause is also in sharp distinction to one following it, which carefully limits the use of video tapes, photographs, and drawings of the operation.

Why the Consent Form Wasn't Better

Writing consent forms by committee is a difficult business. Nevertheless, there are no excuses for the quality of Clark's consent form, only explanations.

The first explanation is that the form's writers opted for a general form that would cover all candidates—even though it was clear from the outset (the FDA had approved seven implants) that unless the first implant was successful, there would be no more for some time. The only blank lines on the form are for the patient's diagnosis, and the members of the surgeon's evaluation committee. The rest is boiler plate.

The second explanation is that the protocol, and thus the consent form, were changed in May 1982, after initial IRB approval in February 1981. The change was needed to expand the pool of potential artificial heart recipients to include those patients, like Dr. Clark, suffering from "chronic nonoperable, end-stage progressive congestive heart failure," because no patients qualified for the implant under the previous protocol.

Finally, the IRB itself seems to have focused on two specific consent issues, almost to the exclusion of others: life style and finances (E. J. Eichwald, "Insertion of the Total Artificial Heart," *IRB: A Review of Human Subjects Research*, August/September 1981). Both are dealt with adequately in the form, although the sections on finances (which require Dr. Clark to assume all financial responsibility) are probably the clearest in the entire document.

Lessons

From the press reports it seems that the consent process used with Dr. Clark was superior to the form that only evidences it. It is also true that Dr. Clark received significantly more information about the permanent artificial heart than did the first recipients of a temporary artificial heart, an artificial heart valve, a primate heart, a human heart, a human kidney, and primate kidney (G. J. Annas, L. H. Glantz, and B. F. Katz, *Informed Consent to Human Experimentation: The Subject's Dilemma*, Ballinger, Cambridge, 1977, pp. 10-18). Surgical procedures are seldom subjected to prior reviews by either IRBs or the FDA. Indeed, of this list of firsts, this is the first that involved such external review. But prior review of ethical and legal considerations took a back seat to the technical aspects of the implant, and the sloppy consent form is merely one piece of evidence supporting this. The debate over Dr. Clark's access to the "key" that he could use to turn off the air compressor is another. Both his ability to use the key should he remain competent, and the conditions under which others should use it if he did not, should have been dealt with *before* the implantation of the artificial heart.

The problem of readable, reliable, and useful consent forms is endemic to the human research enterprise. The fact that IRBs spend the vast majority of their time worrying and debating about the words used in consent forms should disturb those who look to the IRB to protect subjects. The IRB may take the words in consent forms very seriously, but as Charles Bosk has noted, "The quality of the consent obtained is not an issue that excites surgeons or affects their evaluation of each other" (*Forgive and Remember*, University of Chicago Press, 1979, p. 218).

At least in cases of surgical intervention designed to prolong the life of a dying subject, the contents of the consent form seem to be treated as bureaucratic red tape. But forms can be more. Specifically tailored to Barney Clark, and setting forth actions to be taken under reasonably foreseeable developments, "forms" could have provided him a measure of self-determination and dignity now denied him. The opportunity has been lost for Dr. Clark, but not for those who will follow.

Informed Consent to Human Experimentation:

The Subject's Dilemma

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Ballinger Publishing Company • Cambridge, Massachusetts
A Subsidiary of Harper & Row, Publishers, Inc.

1977

ARTIFICIAL HEART EXPERIMENTATION (exerpt from ch. 1)

In April 1969 Dr. Denton Cooley implanted an artificial heart, developed by Dr. Domingo Liotto, in the chest of Haskel Karp. Mr. Karp survived for approximately sixty-four hours on the device, but died about a day after it was replaced by a human donor heart.

After a period of praising Dr. Cooley's efforts to keep her husband alive, Mrs. Karp changed her mind and sued Drs. Cooley and Liotta for malpractice, alleging, among other things, failure to obtain informed consent. A verdict was directed by the trial court in favor of the doctors in October 1972, and affirmed on appeal in April 1974 by the Fifth Circuit of the United States Court of Appeals.[41]

Mrs. Karp's major contention was that Dr. Cooley had failed to obtain adequate informed consent for this exceptional and experimental procedure. At the trial it was established that Dr. Cooley had discussed the procedure with Mr. Karp on at least two occasions, and that Mr. Karp had signed two consent forms on two other occasions. The first form was the hospital's general consent form which he signed upon admission. It read as follows:

> I hereby authorize the physician or physicians in charge of Haskel Karp to administer any treatment; or to administer such anesthetics and perform such operation as may be deemed necessary or advisable in the diagnosis and treatment of this patient.[42]

This is often termed a "blanket" consent form and is usually held by the courts to be insufficient consent for surgical procedures because of its lack of specificity. If Dr. Cooley had relied exclusively upon this consent form he would probably have lost this case instead of winning. About three weeks after hospitalization, however, and prior to the operation, Mr. Karp signed, and Mrs. Karp witnessed, the following consent form:

> I, Haskell Karp, request and authorize Dr. Denton Cooley and such other surgeons as he may designate, to perform upon me, in St. Luke's Episcopal Hospital of Houston, Texas, cardiac surgery for advanced cardiac decompensation and myocardial insufficiency as a result of numerous coronary occlusions. The risk of the surgery has been explained to me. In the event cardiac function cannot be restored by excision of destroyed heart muscle and plastic reconstruction of the ventricle and death seems to be imminent, I authorize Dr. Cooley and his staff to remove my diseased heart and insert a mechanical cardiac substitute. I understand that this mechanical device will not be permanent and ultimately will require replacement by a heart transplant. I realize that this device has been tested in the laboratory but has not been used to sustain a human being and that no assurance of success can be made. I expect the surgeons to exercise every effort to preserve my life through any of these means. No assurance has been made by anyone as to the results that may be obtained.

> I understand that the operating surgeon will be occupied solely with the surgery and that the administration of the anesthetic(s) is an independent function. I hereby request and authorize Dr. Arthur S. Keats, or others he may designate, to administer such anesthetics as he or they may deem advisable.
>
> I hereby consent to the photographing of the operation to be performed, including appropriate portions of my body, for medical, scientific, and educational purposes.[43]

While far superior to the first, there is no suggestion that this form is flawless. It contains a number of medical terms not rendered in lay language (*e.g.*, cardiac decompensation), describes the possibilities of success and failure only in the most general terms, and gives a far broader anesthetic authorization than is necessary. The form also fails to spell out clearly the experimental nature of the artificial heart and the probability of its both being implanted and functioning successfully. There was evidence that Dr. Cooley told Mrs. Karp orally that her husband had a 70–30 chance of surviving the ventriculoplasty (plastic reconstruction of the ventricle) operation.

Mrs. Karp's first allegation, that she did not understand how experimental this procedure was, was rejected as irrelevant. The court noted that under the law only Mr. Karp had the power to consent to this surgery. Her second argument, that her husband did not read the document, was also rejected by the court since Texas law (the law which this federal court had to apply to the case) required that the jury be instructed that Mr. Karp was charged with reading the consent document by the fact of his signature, even though he in fact did not. Her final major argument—and the one which both courts spent most of their time examining—was that Dr. Cooley did not give Mr. Karp sufficient information concerning the nature of the artificial heart to enable Mr. Karp to give a valid informed consent.

While this case involved a first-of-its-kind human experiment done with debatable pretesting on animals and without formal peer review of protocol, these issues were not dealt with by the court. Indeed, the appeals court summarily dismissed the experimentation argument by noting that "the record contains no evidence that Mr. Karp's treatment was other than therapeutic and we agree that in this context an action for experimentation must be measured by traditional malpractice evidentiary standards."[44]

We would argue that while the case points up the great utility of a consent form that at least attempts some specificity, the proposition that this was not primarily an experiment (albeit a "therapeutic" one) is untenable. The court's conclusion can only mean that the judge was not presented with sufficient evidence at the trial level on this issue, or viewed the magnitude of the risks involved as irrelevant.

If the procedure was considered experimental, the court could have properly applied federal Health, Education and Welfare guidelines concerning consent forms, which required at that time—among other things—a complete disclosure of the possible risks and benefits of the experimental procedure.[45]

In this regard it is worthy of note that in 1974 the National Heart and Lung Institute announced supplemental criteria for the human testing of therapeutic devices under its research contracts which include the following:

> The device is to be used only in a situation in which it offers at least as likely benefit as any known accepted technique or any experimental technique which is available for clinical trial in the same setting by the same group.
>
> There must be experimental evidence from laboratory animal studies of beneficial effect.
>
> Definitive criteria for patient selection must be included in the investigation protocol.
>
> The approval of local institutional research committee and other appropriate committees and conformity to the Institutional Guide to DHEW Policy on Protection of Human Subjects is required.
>
> Prior to the clinical use, the complete research protocol must be approved by NHLI.[46]

Anyone currently doing research on human beings whose funding derives from HEW or whose hospital requires institutional review prior to investigation on humans, could be found guilty of malpractice for failure to follow these and other NHLI guidelines. Dr. Cooley's case could have been resolved differently had the court viewed the issue as experimentation rather than therapy. The NHLI Regulations also illustrate how specific a federal agency can get in regulating human experimentation.

The major distinguishing characteristic of the *Karp* case as compared with other first-of-their kind implant and transplant cases was that it got to court. In almost every other example of completely novel surgical intervention of this type, the patient was given less information concerning the procedure than Haskell Karp, and in some instances not even told of the specifics of the procedure, let alone of its highly experimental nature. A few of these cases merit discussion, even though they never reached the courts, because they illustrate many of the problems, both perceived and real, of informed consent to potentially therapeutic experimentation by the terminally ill patient—the one most likely to be the subject of such drastic forms of experimentation.

The first patient to survive the implantation of an artificial heart valve, Mary Richardson, for example, was not even told about the implant prior to the procedure. Instead she was led to believe that the operation was merely a repeat of a more routine one that had previously been performed on her. The surgeon, Dr. Dwight Harkin, not only did not tell her about the procedure (even after the operation), but inaccurately denied that she could hear the clicking sound made by her artificial valve. She did not actually see the type of artificial valve that was used in the procedure until she left the hospital and was confronted by a group of newspaper photographers and a nurse who held the valve in her hands.[47]

While Ruth Tucker, the first recipient of a human kidney, was informed about the nature of the procedure before the operation, the surgeon, Dr. Richard Lawler, refused to tell her that the operation had been a failure. Instead, he made this information known at a medical meeting, and it was transmitted to Ms. Tucker by a reporter, who came to her house to get her reaction to the doctor's report on her case. She is quoted as having said, "What a way to get your death sentence—from a newspaper reporter."[48]

The first recipient of monkey kidneys, Jefferson Davis, a black patient in a New Orleans charity hospital, indicated that he didn't think he had any choice but to accept. In his words, to his surgeon, Dr. Keith Reemtsma, "You told me it gonna be animal kidneys. Well, I ain't got no choice." His wife indicated even less knowledge, "They said, the doctors, that they'd do a transplant, but they never said it'd be a monkey, a chimp, you know. I didn't know that until they did it. When it came out in the papers . . . that's the first I knew about it."[49]

The recipient of the first heart transplant, Boyd Rush, had a similar experience. His sister signed the following consent form:

> I hereby give full permission for left leg amputation and heart surgery on Boyd Rush. I understand that any clots present will be removed from the heart to stop them from going to still more arteries of his body. I further understand that his heart is in extremely poor condition. If for any unanticipated reason the heart should fail completely during either operation and it should be impossible to start it, I agree to the insertion of a *suitable heart transplant* if such should be available at the time. I further understand that hundreds of heart transplants have been performed in laboratories throughout the world but that any heart transplant would represent the *initial transplant in man*. (emphasis supplied)[50]

At the time of the operation no human donor was available so Dr. James D. Hardy performed the heart transplant using a large chimpanzee as a donor. The words "suitable heart" were thought to be broad enough to justify this. The operation was unsuccessful, and the furor in the medical community that it evoked helped insure that the first human heart transplant would not take place in the United States.[51]

The first recipient of a human heart was told about the proposed procedure, but not about the risks it entailed and the probability of success. Instead Dr. Christiaan Barnard purposely led Louis Washkansky to believe that the procedure had an eighty percent success probability, instead of telling him that the eighty percent referred only to his chances of coming out of the operation alive, not to getting better as a result of it.[52] In Dr. Barnard's words:

> He had not asked for odds or any details . . . He was ready to accept it because he was at the end of the line, waiting for a transfer. What else was there to say? Either you got it, or you folded up . . . Since then many people have said it was very brave of Mr. Washkansky to accept a heart transplant. They really mean it would be brave for them to accept a heart transplant—not Washkansky. *For a dying man, it is not a difficult decision because he is at the end.* If a lion chases you to the bank of a river filled with crocodiles, you will leap into the water convinced you have a chance to swim to the other side. But you would never accept such odds if there were no lion.[53] (emphasis supplied)

Barnard did not add, although he could have, that it is much easier to "accept such odds" when they are presented as being heavily in your favor, instead of the way they really are. His view of the dying patient, however, is not uncommon among transplant surgeons, and was echoed later by Dr. Denton Cooley in describing his relationship with Haskell Karp, the case which initiated this discussion: "He was a drowning man. *A drowning man can't be too particular what he's going to use as a possible life preserver*. It was a desperate thing and he knew it."[54] (emphasis supplied)

Heart transplants and the use of artificial hearts or assist devices remain controversial. In response to the attitudes of many thoracic surgeons, and the difficulties of obtaining an informed consent from a dying patient to such experimental procedures, the Committee on Ethics of the American Heart Association in early 1976 published some guidelines regarding the clinical use of the left ventricular assist device (LVAD), a device which is a partially implanted artificial heart for temporary use following some forms of heart surgery. Noting the likelihood of a "strong mutual dependency" existing between the surgeon and the patient, the committee suggested that both the patient and his family may have lost their ability to give a meaningful consent. The cases just reviewed would certainly support this view. Consequently, the committee recommended the participation of a third party in the consent procedure. In the committee's words:

> The participation of a third party, which may be more than one person to mediate the consent process without being caught up in the force of its dependencies ought to make the consent decision more genuine. It should also be a source of reassurance and comfort to both family and paramedical personnel, as well as to the patient and his doctor.[55]

The committee further went on to recommend that in cases where even with this assistance the patient and family are so faced with anxiety and distress as to make the in-depth communication necessary for informed consent impossible, that such patients be excluded from the initial LVAD trials. The committee also explicitly rejected the view that the terminal condition of the patient itself justified the use of this experimental device: "It is insufficient to claim in a narrow context of high-risk treatment that the patient would be dead had he not been revived. The joint context of both innovative therapy and of research ought to comprise an ethical sensitivity to outcome that goes beyond the mere completion of the trial."[56]

* * * * *

SUMMARY AND CONCLUSIONS

1. The most complete and authoritative statement of the law of informed consent to human experimentation is the Nuremberg Code. This Code is part of international common law and may be applied, in both civil and criminal cases, by state, federal and municipal courts in the United States.

2. Almost all of the cases decided by courts concerning experimentation before the enunciation of the Nuremberg Code dealt with experimentation as the equivalent of either rash or ignorant activity, and usually held physicians strictly liable for the consequences of their experiments on patients. All of these cases involved what we would now classify as malpractice or quackery.

3. After World War II the attitude toward human experimentation shifted and courts began to view it as an important and legitimate enterprise, and put emphasis on the necessity of obtaining the patient's informed consent rather than the novelty of the procedure.

4. Examples of "medical firsts" in artificial implants and organ transplantation indicate that the doctrine of informed consent may not be a useful one in terms of protecting the patient's right of self-determination because of the patient's distress and dependency on the surgeon. In such cases it may be appropriate to have a third party or group of persons who act as mediators or patient advocates to insure that the patient understands the procedure and its probable consequences before the patient-subject's consent is obtained.

5. There is no "therapeutic privilege" available to the physician in cases of nontherapeutic experimentation, and all information material to the subject's decision concerning participation must be presented to the subject.

REFERENCES

* * * * *

40. Karp v. Cooley, 349 F. Supp. 827 (S.D. Tex. 1972); Karp v. Cooley, 493 F.2d 408 (5th Cir. 1974).

41. *Id.*

42. Karp v. Cooley, 349 F. Supp. 827, 829 (S.D. Tex. 1972).

43. *Id.* at 831.

44. Karp v. Cooley, 493 F.2d 408, 423 (5th Cir. 1974).

45. *See*, notes 31-32 *supra* and accompanying text.

46. NIH Guide, 3:11 (Aug. 7, 1974).

47. Thorwald, The Patients (1971) at 57-63. Ms. Richardson was the second person to receive an artificial implant at the hands of Dr. Dwight Harkin, and the only one of his first five recipients to survive.

48. *Id.* at 92-101. As reported in the *Chicago Tribune* of May 23, 1951.

49. Thorwald, The Patients (1971) at 200-205.

50. *Id.* at 246.

51. *Id.* at 248-250.

52. Barnard, One Life (1969) at 348.

53. *Id.* at 310-311.

54. Thorwald, The Patients (1971) at 402.

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56. *Id.* at 824.

AT LAW

The Phoenix Heart: What We Have to Lose

by George J. Annas

In the two years following the first human-to-human heart transplant by Dr. Christiaan Barnard, more than 150 heart transplants were performed around the world at 60 different centers. The results were almost uniformly disastrous for the patients. This "unseemly rush to climb on this glamorous bandwagon" club of heart transplanters is one of the darkest episodes in the annals of surgery (B. Jennett, *High Technology Medicine*, London, 1984). Did we learn anything from it, or are heart surgeons around the world poised to repeat this exercise in premature human experimentation, this time using artificial hearts?

Repetition does not seem likely with permanent artificial hearts, since the results of experiments to date have been so devastating to the patients. Use of the artificial heart as a *temporary* measure, however, is gaining support; thoughtful planning will be needed to prevent another round of indiscriminate experimentation.

The Phoenix Heart Implant

On Tuesday morning, March 5, 1985, Dr. Jack Copeland, Chief of University Medical Center's Heart Transplant Team in Tucson, Arizona, performed a human heart transplant on Thomas Creighton, a thirty-three-year-old, divorced father of two. Copeland later explained that the donor, an accident victim who had been hospitalized for several days, "wasn't what we'd call an excellent donor candidate (but in view of the urgency) we elected to proceed with the transplant" (*Arizona Daily Star*, March 7, 1985, p. 2). The procedure was not a success, because of rejection of the heart. At 3:00 a.m. Wednesday a search for another human heart began; Mr. Creighton was placed on a heart-lung machine.

At 5:30 a.m. a call was placed to Dr. Cecil Vaughn of Phoenix, asking if he had an artificial heart ready for human use. Dr. Vaughn was scheduled to implant an experimental model developed by dentist Kevin Cheng into a calf later that day, but had never considered use of the device in a human. Nonetheless, he called Dr. Cheng. Dr. Cheng told him, "It's designed for a calf and not ready for a human yet." Asked to think about it for ten minutes, Dr. Cheng recalls, "I knelt and prayed." When Vaughn called him back he said, "The pump is sterile, ready to go" (*New York Times*, March 19, 1985, pp. C1-C2).

The two flew by helicopter from the hospital to the airport, chartered a jet to Tucson, and then took another helicopter to the Tucson hospital. They arrived at 9:30 a.m. Wednesday. The implant procedure began at noon. Designed for a calf, the device was too large, and the chest could not be closed around it. The implant maintained circulation until 11:00 that night when, in preparation for a second heart transplant, it was turned off, and Mr. Creighton was put back on the heart-lung machine. By 3:00 a.m. Thursday, the second human heart transplant was completed. The next day Mr. Creighton died.

The press treated the story like a modern American melodrama. *USA Today* called the implantation of Dr. Cheng's device "the fulfillment of an American dream" (March 8, 1985, p. 1A). The *New York Times* editorialized that "the artificial heart has at last proved it has a useful role..." (March 9, 1985, p. 22). *Newsweek* faulted the FDA, noting, "Its hardly fair to doctors, or their patients, to make them break the law to save a life" (March 18, 1985, pp. 86-88). The FDA initially termed the unauthorized experiment a violation of the law, but by week's end had done an about face and was flailing itself as "part of the problem" (*New York Times*, March 17, 1985, p. 87).

Melodrama calls on us to suspend our critical judgment, identify with the protagonists, and join emotionally in the drama. This may be an appropriate response to soap operas, but we need to take a rational view of the events in Arizona—not to judge the actors in that drama, but to decide what transplant policies we should now pursue.

Justifications for the Implant

The physicians and their supporters have given three basic justifications for the implant: (1) the "only other option was just to let him die" so "we had nothing to lose"; (2) in an emergency, a physician can do anything to save the patient's life; and (3) FDA regulations do not apply to dying patients. None of these excuses can survive scrutiny.

A matter of life or death: Dr. Copeland has justified the incident primarily by saying, we had "nothing to lose" by trying the artificial heart (*Arizona Daily Star*, March 8, 1985, pp. 1-2). Dr. William DeVries also used this justification for Barney Clark's permanent implant.

But the choices were not just "live or die." The reality was closer to: "Accept the implant and you'll almost certainly die anyway; and if you do live, you could spend the rest

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of your life severely disabled, mentally and physically." When the possibility of a "halfway success," survival in a severely impaired state, is added to the equation, the patient has much to lose, including his self-determination and dignity as a human being.

The Arizona implant was not performed in isolation, but as a response to an unsuccessful human heart transplant. In planned procedures like transplants, only the patient should be permitted to decide whether to resort to extreme and experimental methods of maintaining life, like artificial hearts. That Mr. Creighton was not the person who made this decision raises the question of what he was led to expect from the heart transplant, what risks (including the risk of rejection) were explained to him, and what steps he had agreed to should any of the risks materialize. Proxy consent (reportedly obtained from the patient's mother and sister) is inadequate to justify extreme experimentation, unnecessary for emergency therapy, and irrelevant if quackery is involved.

Taken to its logical extreme, the "nothing to lose" excuse can justify *any* experiment on a dying patient "to save the patient's life." The "right to die with dignity" movement is only one reaction to this type of thinking. This excuse also embodies a "magical" myth: that the physician has the power to conquer death and that prolonging life is *always* a reasonable goal. As psychiatrist Jay Katz of Yale Law School has noted in another context in his book *The Silent World of Doctor and Patient* (New York, Free Press, 1984):

> At such times, all kinds of senseless interventions are tried in an unconscious effort to cure the incurable magically through a "wonder drug," a novel surgical procedure, or a penetrating psychological interpretation...The doctors' heroic attempts to try anything...may turn out to be a projection of their own needs onto patients (p. 151).

The emergency justification: University officials justified the incident on the basis that physicians are privileged to do anything they believe is appropriate in a medical emergency. This is wide of the mark. The emergency rule is, "treat first, and ask *legal* questions later." Thus an emergency situation may justify a physician's decision not to review federal regulations prior to acting, but it can never justify a physician in not considering *medical* data before acting. The medical "reasonableness" of using the artificial heart in a true emergency is debatable. But was this a true, unanticipated, emergency?

Organ rejection is a known risk of all transplant procedures. Mr. Creighton was Dr. Copeland's third patient to suffer immediate heart rejection. He vowed after the second to do all he could to save the next such patient. Thus, not only is organ rejection a "reasonably foreseeable risk" of transplantation, Dr. Copeland knew of this risk firsthand and had ample opportunity to develop a plan to deal with the next case he encountered. Under these circumstances organ rejection is not an unanticipated "emergency" that justifies unthought out, extreme interventions.

FDA approval: The press tended to use the Arizona incident as an illustration of how government regulation doesn't work; and, unfortunately, the FDA seems to agree, to the point of almost apologizing for its own existence. The life-or-death and emergency excuses would equally justify the use of unapproved drugs like laetrile on dying cancer patients by licensed or unlicensed practitioners, and could be used to justify an artificial heart implant by an unlicensed practitioner. The FDA cannot sanction these types of reckless behaviors.

As the U.S. Supreme Court noted in upholding the FDA's authority over laetrile, "To accept the proposition that the safety and efficacy standards of the Food, Drug & Cosmetic Act have no relevance for terminal patients is to deny the Commissioner's authority over all drugs, however toxic or ineffectual, for such individuals...[the terminally ill deserve protection] from the vast range of self-styled panaceas that inventive minds can devise" (U.S. v. Rutherford, 544 U.S. 442, 1979).

Even if *all* physicians opposed reasonable regulation of the safety and efficacy of drugs and medical devices, the FDA should not apologize for the important role Congress has assigned to it in protecting the public against unsafe, untested, and useless medical devices. Dr. Copeland's argument that not to use the device would have made "the government his executioner (*USA Today*, March 11, 1985, p. 10A) cannot be taken seriously. Mr. Creighton would have died not from an FDA rule, but from an unsuccessful heart transplant. The FDA properly forbade the "emergency" use of devices that have not been approved even for human experimentation, and should continue to do so.

In short, the unplanned use of unapproved temporary artificial hearts is not justified. But the planned use of approved temporary artificial hearts is problematic as well.

Reconsidering the Queue

Before we commit ourselves to more experimentation with the artificial heart as a temporary device, as is currently planned at the Hershey Medical center in Pennsylvania, it seems reasonable to anticipate how use of such devices should fit into the broader area of heart transplantation and organ rationing. (See George J. Annas, "Regulating the Introduction of Heart and Liver Transplantation," *American Journal of Public Health*, 15:93, 1985).

The use of "medical urgency" as a justification for "jumping the queue" is problematic. If temporary artificial hearts are used in individuals who are *least* likely to survive human heart transplants and be rehabilitated, thus taking away organs from those who are most likely to benefit, this new technology will not "save lives." Instead, its use will indirectly lead to the deaths of individuals on waiting lists. In short, we must recognize that while the shortage of human hearts for transplant exists, temporary artificial hearts will likely do more harm than good.

We should deal with these issues directly; we all have a lot to lose from an incoherent introduction of temporary artificial hearts.

AT LAW

No Cheers for Temporary Artificial Hearts

by George J. Annas

It is no accident that the press and hospitals alike have adopted the sports metaphor for artificial heart implants. Americans love the spectacle of sports, and the combination of life-or-death outcomes and desperate searches for organs from accident victims is almost irresistible. Both hospitals and newspaper writers gain a large and sympathetic audience: large because drama overwhelms reality; sympathetic because we are all cheering the team that challenges death.

In a recent column I argued that temporary experimental artificial hearts could not be justified by saying we have "nothing to lose" or by arguing that FDA approval is not necessary when dealing with dying patients (George J. Annas, "The Phoenix Heart: What We Have to Lose," *Hastings Center Report*, June 1985, pp. 15-16). Nevertheless, the FDA has decided not to regulate the use of temporary artificial hearts, and we are on the verge of an unparalleled free-for-all in human experimentation. This column continues that discussion.

The Sporting Life

Michael Drummond, the first recipient of an FDA-approved artificial heart as a bridge to transplant (the fourth "bridge" recipient in history), was referred to the University of Arizona Hospital for evaluation for possible heart transplant on Monday, August 26. He was listed as a candidate for a human heart transplant on Tuesday, when the possibility of the artificial heart was mentioned for the first time. Early Thursday morning, because Dr. Jack Copeland and others decided Drummond had only forty-eight hours to live, he and his family were reportedly given an option: wait for a human heart transplant and die if one did not become available, or go ahead with an artificial heart implant. They opted for the latter because, as his mother put it, "We had no choice."

The patient himself had no clear idea what he was consenting to. When he awoke from the procedure, his first words were, "What's this clunking" [in my chest]? The operator of the drive system for his artificial heart, who was present, said he doubted that Mr. Drummond "really understands totally the artificial heart and what it is" [referring to the tubes, drive lines, console and, he could have added, the generators] (*New York Times*, September 2, 1985, p. 10). In addition, after his human heart transplant, Mr. Drummond was enthusiastic about the artificial heart, but reiterated that there was "no alternative" and said he thought he "only had four days to live" (*New York Times*, September 15, 1985, p. 33).

All these statements are troublesome, but not surprising. The consent process was not well thought out at Arizona. The FDA-"approved" consent form, for example, is the most misleading, rudimentary, and confusing one yet used for a total artificial heart implant. It describes the five previous permanent implants as having been done "successfully," with no further explanation of what is meant by this term. It incorrectly states that the Symbion [Jarvik-7] heart is attached "to a portable external drive console which powers the heart with compressed air" when, in fact, the portable drive system was not available at Arizona. It incorrectly states that "it is the *only alternative* which is available to maintain life until a suitable donor heart is found" (emphasis added). And it makes *no* provision for how the patient will die if a human heart transplant is not feasible, or who will make decisions for the patient, and on what basis, if the patient is unable to make them.

Indeed, although the form acknowledges that complications may preclude a human heart transplant, and assures the patient that "you will be supported by the artificial heart as long as possible," it does not explain how this will be done, and Arizona has made no provisions for so supporting a patient (such as the apartment and use of a portable drive available to William Schroeder at Humana Heart Institute).

No wonder Mr. Drummond wanted to know where all the noise was coming from. We may never know if he had four days to live (as he apparently believed) or two days (as his physician apparently believed), but we do know that he did have an alternative (even if he and his family did not think they had one). That alternative was to have his urgency status on the human heart transplant registry upped to "category 9," a category that usually includes only those patients expected to live forty-eight hours or less. This strategy would have provided him with a reasonable chance (though no guarantee) to obtain a human heart initially, without having to undergo the artificial heart implant. There was a significant fail-

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ure of communication if he and his family did not understand this option.

The Transplant

On September 8, two "sporting events" were covered on the front page of the Sunday *New York Times*. Hana Mandlikova defeated Martina Navratilova in the finals of the U.S. Open, and Mr. Drummond received a human heart. Reporter Lawrence K. Altman, who has been the chronicler of artificial heart implants, took full advantage of the sports metaphor. Both his opening sentence and the headline for the story inaccurately described a "new human heart" (it was, of course, a "used" one) brought to Arizona after doctors "raced for seven hours to and from Tyler, Texas."

The sole photograph accompanying the article shows a technician running with the heart in a cooler. Dr. Altman describes the scene at the finish line: "A team member carrying the cooler sprinted across the parking lot to the hospital and was greeted by cheers from surgeons and nurses in the operating room." After the procedure, there was also the thrill of victory, Dr. Robert Vaughn describing the experience as "the thrill of a professional lifetime." Dr. Altman reported hospital spokesperson Nina Trasoff as saying, "[Drummond] watched some of the tennis matches yesterday and some football, and he's anxious for the tennis and football to get underway this morning so he can watch some more" (*New York Times*, September 2, 1985, p. 10).

Experimentation is being turned into a sporting event and a spectator sport. As a sporting event it has no rules (since the FDA and NIH have abdicated any role as referee). As a spectator sport it is the most gruesome and morbid type of entertainment.

What If It Works?

As long as there is a shortage of transplantable human hearts, temporary artificial hearts that predictably "work" can serve *no useful purpose*, and are potentially destructive of important human values. Most heart transplant surgeons realize this, and that is why they are not rushing to adopt this "new technology." But the pressure to adopt it from an uninformed public, easily impressed by flash and drama, may make the technology difficult to resist. Accordingly, it is important to understand the argument.

First, as long as there is a shortage of transplantable human hearts, *temporary* artificial hearts cannot increase the total number of human heart transplants performed; they can only change the identity of the individuals who obtain them. For example, assume hypothetically that we have 1,000 individuals annually qualified for human heart transplants in the U.S. and that 600 human hearts are available. The remaining 400 will not receive a heart and will therefore die. If before their deaths these 400 are put on artificial hearts, the "waiting pool" will increase to 1400 next year, although only 600 hearts will be available. If priority is given to those on artificial hearts, these 400 will get hearts, but only 200 of the 1000 remaining on the list will get them. If the remaining 800 are not to die, they will get temporary artificial hearts. But this will already outstrip the next year's supply of human hearts. Six hundred will get them, 200 will wait another year, and the new group of 1000 potential recipients will either all die, or will have to get "temporary" hearts that will actually be "permanent" for most of them.

If we could dramatically increase the total number of available human hearts, or decrease the number of candidates, this scenario could change, but there is *no* reasonable expectation of this happening. Until there is, this technology merely increases the total cost of doing human transplants on the same number of patients. It also leaves us with a significant number of patients on artificial hearts that were believed to be temporary, but have become permanent. Since we have *no* policy or plan concerning what to do with them or how to make decisions about complications or turning off their artificial hearts, it is unethical even to begin this process.

In addition to being useless to society as a whole, temporary artificial hearts are unfair to those other patients on the waiting list for a human heart, at least if temporary artificial heart recipients are given priority over all others. After the artificial heart implant, Mr. Drummond was placed in category 9, the most urgent, although his hospital admitted he did not meet the criteria for that category since he was not expected to live forty-eight hours or less without the human heart. According to a hospital spokesperson, the *only* reason he was thought to qualify for that category was "because of the history of the Jarvik [7], it is felt that he is in fact in imminent danger of death because of that potential for stroke" (*New York Times*, September 7, 1985, p. 7). It is possible that because Mr. Drummond obtained the human heart on the basis of his "category 9" status and the intense national publicity surrounding his case, someone else in category 9—someone who really was dying imminently—did die. Whether or not this actually happened in the Drummond case, there is no doubt that if more temporary hearts are used, and if the hospitals that use them manipulate the procurement system to have recipients placed at the top of the priority list, others will die.

We need a moratorium on permanent artificial hearts because of the devastating effects they have had on their recipients. We need a moratorium on temporary artificial hearts because there is no guarantee they will not be permanent, we have yet to develop an ethically acceptable method of allocating human hearts to those with artificial hearts, and there is no room in our health care system for an extreme and expensive medical technology that is useless because it does not increase the total number of human lives saved by heart transplants.

If the referee won't call time out, the players themselves should.

AMERICAN JOURNAL OF Public Health reprint

Public Health and the Law

The Prostitute, the Playboy, and the Poet: Rationing Schemes for Organ Transplantation

GEORGE J. ANNAS, JD, MPH

In the public debate about the availability of heart and liver transplants, the issue of rationing on a massive scale has been credibly raised for the first time in United States medical care. In an era of scarce resources, the eventual arrival of such a discussion was, of course, inevitable.[1] Unless we decide to ban heart and liver transplantation, or make them available to everyone, some rationing scheme must be used to choose among potential transplant candidates. The debate has existed throughout the history of medical ethics. Traditionally it has been stated as a choice between saving one of two patients, both of whom require the immediate assistance of the only available physician to survive.

National attention was focused on decisions regarding the rationing of kidney dialysis machines when they were first used on a limited basis in the late 1960s. As one commentator described the debate within the medical profession:

> "Shall machines or organs go to the sickest, or to the ones with most promise of recovery, on a first-come, first-served basis; to the most 'valuable' patient (based on wealth, education, position, what?); to the one with the most dependents; to women and children first; to those who can pay; to whom? Or should lots be cast, impersonally and uncritically?"[2]

In Seattle, Washington, an anonymous screening committee was set up to pick who among competing candidates would receive the life-saving technology. One lay member of the screening committee is quoted as saying:

> "The choices were hard . . . I remember voting against a young woman who was a known prostitute. I found I couldn't vote for her, rather than another candidate, a young wife and mother. I also voted against a young man who, until he learned he had renal failure, had been a ne'er do-well, a real playboy. He promised he would reform his character, go back to school, and so on, if only he were selected for treatment. But I felt I'd lived long enough to know that a person like that wouldn't really do what he was promising at the time."[3]

When the biases and selection criteria of the committee were made public, there was a general negative reaction against this type of arbitrary device. Two experts reacted to the "numbing accounts of how close to the surface lie the prejudices and mindless cliches that pollute the committee's deliberations," by concluding that the committee was "measuring persons in accordance with its own middle-class values." The committee process, they noted, ruled out "creative nonconformists" and made the Pacific Northwest "no place for a Henry David Thoreau with bad kidneys."[4]

To avoid having to make such explicit, arbitrary, "social worth" determinations, the Congress, in 1972, enacted legislation that provided federal funds for virtually all kidney dialysis and kidney transplantation procedures in the United States.[5] This decision, however, simply served to postpone the time when identical decisions will have to be made about candidates for heart and liver transplantation in a society that does not provide sufficient financial and medical resources to provide all "suitable" candidates with the operation.

There are four major approaches to rationing scarce medical resources: the market approach; the selection committee approach; the lottery approach; and the "customary" approach.[1]

The Market Approach

The market approach would provide an organ to everyone who could pay for it with their own funds or private insurance. It puts a very high value on individual rights, and a very low value on equality and fairness. It has properly been criticized on a number of bases, including that the transplant technologies have been developed and are supported with public funds, that medical resources used for transplantation will not be available for higher priority care, and that financial success alone is an insufficient justification for demanding a medical procedure. Most telling is its complete lack of concern for fairness and equity.[6]

A "bake sale" or charity approach that requires the less financially fortunate to make public appeals for funding is demeaning to the individuals involved, and to society as a whole. Rationing by financial ability says we do not believe in equality, but believe that a price can and should be placed on human life and that it should be paid by the individual whose life is at stake. Neither belief is tolerable in a society in which income is inequitably distributed.

The Committee Selection Process

The Seattle Selection Committee is a model of the committee process. Ethics Committees set up in some hospitals to decide whether or not certain handicapped newborn infants should be given medical care may represent another.[7] These committees have developed because it was

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seen as unworkable or unwise to explicitly set forth the criteria on which selection decisions would be made. But only two results are possible, as Professor Guido Calabrezi has pointed out: either a pattern of decision-making will develop or it will not. If a pattern does develop (e.g., in Seattle, the imposition of middle-class values), then it can be articulated and those decision "rules" codified and used directly, without resort to the committee. If a pattern does not develop, the committee is vulnerable to the charge that it is acting arbitrarily, or dishonestly, and therefore cannot be permitted to continue to make such important decisions.[7]

In the end, public designation of a committee to make selection decisions on vague criteria will fail because it too closely involves the state and all members of society in explicitly preferring specific individuals over others, and in devaluing the interests those others have in living. It thus directly undermines, as surely as the market system does, society's view of equality and the value of human life.

The Lottery Approach

The lottery approach is the ultimate equalizer which puts equality ahead of every other value. This makes it extremely attractive, since all comers have an equal chance at selection regardless of race, color, creed, or financial status. On the other hand, it offends our notions of efficiency and fairness since it makes *no* distinctions among such things as the strength of the desires of the candidates, their potential survival, and their quality of life. In this sense it is a mindless method of trying to solve society's dilemma which is caused by its unwillingness or inability to spend enough resources to make a lottery unnecessary. By making this macro spending decision evident to all, it also undermines society's view of the pricelessness of human life. A first-come, first-served system is a type of natural lottery since referral to a transplant program is generally random in time. Nonetheless, higher income groups have quicker access to referral networks and thus have an inherent advantage over the poor in a strict first-come, first-served system.[8,9]

The Customary Approach

Society has traditionally attempted to avoid explicitly recognizing that we are making a choice not to save individual lives because it is too expensive to do so. As long as such decisions are not explicitly acknowledged, they can be tolerated by society. For example, until recently there was said to be a general understanding among general practitioners in Britain that individuals over age 55 suffering from end-stage kidney disease not be referred for dialysis or transplant. In 1984, however, this unwritten practice became highly publicized, with figures that showed a rate of new cases of end-stage kidney disease treated in Britain at 40 per million (versus the US figure of 80 per million) resulting in 1500–3000 "unnecessary deaths" annually.[10] This has, predictably, led to movements to enlarge the National Health Service budget to expand dialysis services to meet this need, a more socially acceptable solution than permitting the now publicly recognized situation to continue.

In the US, the customary approach permits individual physicians to select their patients on the basis of medical criteria or clinical suitability. This, however, contains much hidden social worth criteria. For example, one criterion, common in the transplant literature, requires an individual to have sufficient family support for successful aftercare. This discriminates against individuals without families and those who have become alienated from their families. The criterion may be relevant, but it is hardly medical.

Similar observations can be made about medical criteria that include IQ, mental illness, criminal records, employment, indigency, alcoholism, drug addiction, or geographical location. Age is perhaps more difficult, since it may be impressionistically related to outcome. But it is not medically logical to assume that an individual who is 49 years old is necessarily a better medical candidate for a transplant than one who is 50 years old. Unless specific examination of the characteristics of older persons that make them less desirable candidates is undertaken, such a cut off is arbitrary, and thus devalues the lives of older citizens. The same can be said of blanket exclusions of alcoholics and drug addicts.

In short, the customary approach has one great advantage for society and one great disadvantage: it gives us the illusion that we do not have to make choices; but the cost is mass deception, and when this deception is uncovered, we must deal with it either by universal entitlement or by choosing another method of patient selection.

A Combination of Approaches

A socially acceptable approach must be fair, efficient, and reflective of important social values. The most important values at stake in organ transplantation are fairness itself, equity in the sense of equality, and the value of life. To promote efficiency, it is important that no one receive a transplant unless they want one and are likely to obtain significant benefit from it in the sense of years of life at a reasonable level of functioning.

Accordingly, it is appropriate for there to be an initial screening process that is based *exclusively* on medical criteria designed to measure the probability of a successful transplant, i.e., one in which the patient survives for at least a number of years and is rehabilitated. There is room in medical criteria for social worth judgments, but there is probably no way to avoid this completely. For example, it has been noted that "in many respects social and medical criteria are inextricably intertwined" and that therefore medical criteria might "exclude the poor and disadvantaged because health and socioeconomic status are highly interdependent."[11] Roger Evans gives an example. In the End Stage Renal Disease Program, "those of lower socioeconomic status are likely to have multiple comorbid health conditions such as diabetes, hepatitis, and hypertension" making them both less desirable candidates and more expensive to treat.[11]

To prevent the gulf between the haves and have nots from widening, we must make every reasonable attempt to develop medical criteria that are objective and independent of social worth categories. One minimal way to approach this is to require that medical screening be reviewed and approved by an ethics committee with significant public representation, filed with a public agency, and made readily available to the public for comment. In the event that more than one hospital in a state or region is offering a particular transplant service, it would be most fair and efficient for the individual hospitals to perform the initial medical screening themselves (based on the uniform, objective criteria), but to have all subsequent non-medical selection done by a method approved by a single selection committee composed of representatives of all hospitals engaged in the particular transplant procedure, as well as significant representation of the public at large.

As this implies, after the medical screening is performed, there may be more acceptable candidates in the "pool" than there are organs or surgical teams to go around. Selection among waiting candidates will then be necessary. This situation occurs now in kidney transplantion, but since the organ matching is much more sophisticated than in hearts and livers (permitting much more precise matching of organ and recipient), and since dialysis permits individuals to wait almost indefinitely for an organ without risking death, the situations are not close enough to permit use of the same matching criteria. On the other hand, to the extent that organs are specifically tissue- and size-matched and fairly distributed to the best matched candidate, the organ distribution system itself will resemble a natural lottery.

When a pool of acceptable candidates is developed, a decision about who gets the next available, suitable organ must be made. We must choose between using a conscious, value-laden, social worth selection criterion (including a committee to make the actual choice), or some type of random device. In view of the unacceptability and arbitrariness of social worth criteria being applied, implicitly or explicitly, by committee, this method is neither viable nor proper. On the other hand, strict adherence to a lottery might create a situation where an individual who has only a one-in-four chance of living five years with a transplant (but who could survive another six months without one) would get an organ before an individual who could survive as long or longer, but who will die within days or hours if he or she is not immediately transplanted. Accordingly, the most reasonable approach seems to be to allocate organs on a first-come, first-served basis to members of the pool but permit individuals to "jump" the queue if the second level selection committee believes they are in immediate danger of death (but still have a reasonable prospect for long-term survival with a transplant) and the person who would otherwise get the organ can survive long enough to be reasonably assured that he or she will be able to get another organ.

The first-come, first-served method of basic selection (after a medical screen) seems the preferred method because it most closely approximates the randomness of a straight lottery without the obviousness of making equity the only promoted value. Some unfairness is introduced by the fact that the more wealthy and medically astute will likely get into the pool first, and thus be ahead in line, but this advantage should decrease sharply as public awareness of the system grows. The possibility of unfairness is also inherent in permitting individuals to jump the queue, but some flexibility needs to be retained in the system to permit it to respond to reasonable contingencies.

We will have to face the fact that should the resources devoted to organ transplantation be limited (as they are now and are likely to be in the future), at some point it is likely that significant numbers of individuals will die in the pool waiting for a transplant. Three things can be done to avoid this: 1) medical criteria can be made stricter, perhaps by adding a more rigorous notion of "quality" of life to longevity and prospects for rehabilitation; 2) resources devoted to transplantation and organ procurement can be increased; or 3) individuals can be persuaded not to attempt to join the pool.

Of these three options, only the third has the promise of both conserving resources and promoting autonomy. While most persons medically eligible for a transplant would probably want one, some would not—at least if they understood all that was involved, including the need for a lifetime commitment to daily immunosuppression medications, and periodic medical monitoring for rejection symptoms. Accordingly, it makes public policy sense to publicize the risks and side effects of transplantation, and to require careful explanations of the procedure be given to prospective patients *before* they undergo medical screening. It is likely that by the time patients come to the transplant center they have made up their minds and would do almost anything to get the transplant. Nonetheless, if there are patients who, when confronted with all the facts, would voluntarily elect not to proceed, we enhance both their own freedom and the efficiency and cost-effectiveness of the transplantation system by screening them out as early as possible.

Conclusion

Choices among patients that seem to condemn some to death and give others an opportunity to survive will always be tragic. Society has developed a number of mechanisms to make such decisions more acceptable by camouflaging them. In an era of scarce resources and conscious cost containment, such mechanisms will become public, and they will be usable only if they are fair and efficient. If they are not so perceived, we will shift from one mechanism to another in an effort to continue the illusion that tragic choices really don't have to be made, and that we can simultaneously move toward equity of access, quality of services, and cost containment without any challenges to our values. Along with the prostitute, the playboy, and the poet, we all need to be involved in the development of an access model to extreme and expensive medical technologies with which we can live.

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Mr. VOLKMER. Thank you very much, Doctor Annas.

And Dr. DeVries.

Dr. DEVRIES. Thank you.

Members of Congress, I appreciate the opportunity to present the following comments and observations on the status of the artificial heart program at Humana International. The subcommittee's invitation is representative of a widespread interest throughout the country and world in this program.

I am amazed by some of the consequences of this intense interest. Uninformed public opinion and the trend toward bureaucratic overregulation are a real impediment to scientific progress.

These influences have taken an inordinate amount of time away from the scientific inquiry and the clinical care of artificial heart patients, Bill Schroeder and Murray Hayden. Therefore, I welcome this forum as a chance to set forth my views and respond to questions.

I hope the availability of these proceedings, as well as the protocol modification submitted to the FDA advisory panel, will satisfy public, regulatory, and scientific interests, and facilitate getting on with the project.

The ultimate goal of the artificial heart project is to develop therapy that will be safe and effective in treating patients with end-stage heart disease.

In its long history of conception, research, and development, the program at Audubon has been monitored at various times by one or more of the following groups:

No. 1, a recipient evaluation committee at the hospital where I am principal investigator; (2) the project evaluation committee; (3) the Humana National Advisory Board on total artifical heart, appointed by Humana to oversee comments on ethical and legal aspects of the problem; (4) the institutional review board at Audubon Humana Hospital; (5) the FDA; (6) the FDA advisory panel, the National Institutes of Health, who supported the initial investigation of the heart through grants in the 1960's and 1970's, and continues to support nonclinical research, and Symbion, manufacturer of Jarvik-7, which I have used in four implants I have performed.

I would like to consider this hearing as a positive step in establishing a dialog as to what type of scientific and societal oversight is realistic and reasonable. This oversight should insure No. 1, that the clinical and scientific integrity of the project is maintained. No. 2, the patient is adequately informed. And No. 3, the risk-to-benefit ratio is such that the value of scientific information to be obtained justifies the exposure of the patient to potential complications.

I willingly invite the dialog with the FDA, the subcommittee and others, as to what constitutes realistic, reasonable, and appropriate monitoring. And what constitutes adequate scientific progress.

Oversight by one's scientific and clinical peers is indispensible, provided they are appropriately knowledgeable and responsible. In addition, some type of conscientious societal oversight can serve a very useful purpose.

All these monitoring processes should be applied uniformally and consistently to all implantation centers, regardless of whether the center is academic or proprietary. Clinical experience with the artificial heart has yielded a tremendous wealth of scientific information. Valuable data concerning strokes, hemostasis, thrombosis, hemodynamics, and immunology have been derived from my patients.

Some of this data offers the exciting prospect of spinoff of advances for related areas of medicine. In addition, the program's contribution to public awareness and education as be related to media coverage, is an incalculable benefit.

I think the average American is better informed about heart disease in general, its risk factors, organ donation, and a variety of related issues as a result of the artificial heart project.

Artificial heart recipients fall into two groups. Permanent and temporary—bridge-to-transplant.

Patients may go from one group to another as medical indications change. Of the four implants I have performed all have been permanent.

The first was done at the University of Utah on December 1, 1982; the patient was Barney Clark. He lived 112 days.

The patients at Humana Heart Institute International have been William Schroeder, alive now 438 days; Murray Haydon, alive now 354 days; and Jack Burcham, who died after 10 days.

When my results are compared with other medical experiments at similar or investigational stages they are encouraging.

Based on length of life alone, the artificial heart is an astonishing scientific achievement.

The long-survival rate of artificial heart recipients has gained added significance when their nearness to death at the time of the implantation is recalled. As with all early medical studies, we had to surmount many obstacles.

Mr. Schroeder continues to recover from the stroke suffered November 10, which necessitated his return to the hospital.

He is now undergoing physical occupational speech therapy. Although he is not as active as he was before his stroke he is able to stand, walk, and recognize family members, friends and hospital staff, and to speak a few words. I have seen him like this on two previous strokes and both times he made remarkable progress. I believe he will do so again.

Mr. Haydon has had no neurological damage. He experienced a mild transient stroke in June and remains in the hospital because of the dependence on a respirator. He is gradually being weaned from the respirator, and remains very weak.

He is moving about the hospital, and yet the day before yesterday he visited his home for the weekend. We are very encouraged by Mr. Haydon's postoperative course.

If Mr. Schroeder had been the only recipient we might have been tempted to conclude that debilitating strokes are a necessary consequence of the heart. But you only have to walk down the hall to Mr. Haydon's room to see that simply is not the case.

Do Bill Schroeder and Murray Haydon have the quality of life they want, or you want for them?

Probably not.

Is their quality of life adequate considering their preoperative state?

Absolutely.

Mr. Chairman, as a physician, I would not implant an artificial heart if I did not think I would give the patient increased quality of life. And it has.

Bill and Murray would be dead if they did not have the artificial heart.

Neither of them have asked me to turn off the Utahdrive and end his life. Nor has Juanita Haydon or Margaret Schroeder asked for this, although I have discussed this possibility at length with each of them, and I will continue to do so.

Although I want Bill Schroeder and Murray Haydon to live normal lives, we must bear in mind that the project is an early clinical investigation. All patients accepted this fact before entering the project.

A principal investigator has to have an adequate patient base to make a wise and prudent decision as to whether an investigational procedure is worthwhile. The artificial heart is still an experimental device.

There have not been enough recipients to make a good decision on its safety and efficacy. I am encouraged to see other institutions cooperating in artificial heart research. But clinical trials are still few in number.

No other experiment in the history of science has been scrutinized so closely as this one. Such close attention has led to a case-by-case mentality and a tendency to judge the experiment in terms of how the most recent artificial heart recipient is doing.

This mentality, although understandable and well intended, is a threat to the scientific progress of this or any other research project. Had many experiments in the history of science been subject to such close scrutiny they might well all have been stopped. The medical advances they produce could not have been made for many years or might not have occurred at all. Spinoff advancement which recently came about as a direct result of perceived failures would have been permanently lost to science and to mankind.

Appropriate and reasonable scientific and societal monitoring of the artificial heart project can be useful. However, regulatory bodies should evaluate a project based on an appropriate scientific reporting and timely publications by the investigator, not by media presentations.

In conclusion, what is the real nature of the artificial heart project?

It is clinical research; but it is also a microcosm of life, involving a number of important domains. It touches on legal issues of patients consent, the right to live and the right to die.

It touches on family responsibilities for patients who are very ill. It is an experiment with as many soft data points as hard ones.

To say the only thing we are learning in this project is whether the artificial heart will pump or will not, is to grossly undervalue its usefulness, and minimize its many potential benefits to society.

Thank you, Mr. Chairman, for the opportunity of opening this dialogue.

[Additional questions and answers for the record and the prepared statement of Dr. William C. DeVries follow:]

ADDITIONAL QUESTIONS AND ANSWERS FOR THE RECORD

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE AND TECHNOLOGY
SUITE 2321 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-6371

ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
HARRIS W. FAWELL, Illinois
WILLIAM W. COBEY, JR., North Carolina
JOE BARTON, Texas
D. FRENCH SLAUGHTER, JR., Virginia
DAVID S. MONSON, Utah

HAROLD P. HANSON
Executive Director
ROBERT C. KETCHAM
General Counsel
JOYCE GROSS FREIWALD
Republican Staff Director

April 7, 1986

Dr. William C. DeVries
Artificial Heart Program
Humana Heart Institute International
1 Audubon Plaza Dr.
Louisville, KY 40217

Dear Dr. DeVries:

Enclosed is a copy of the transcript from the February 5, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight about artificial hearts. Attached to the transcript are instructions for submitting requests for changes or clarifications. Please review these instructions and the enclosed transcript of your remarks carefully.

The Subcommittee would also appreciate your written responses to the following questions:

1. In February, you were planning to submit a revised informed consent form to the FDA. Please inform us whether you have done so and whether FDA has approved the proposed informed consent form.
    - How does the proposed consent form reflect the information learned from your experiences with the first four patients who received permanent artificial hearts?
    - Does the proposed consent form include provisions for alternative decision-making should the patient become incompetent or unable to communicate?
    - What is the status of proposed legislation in the Commonwealth of Kentucky to allow family members to participate in the decision making process?

2. It has been suggested that a multi-center review panel be formed to develop uniform standards related to the artificial heart implant protocol, patient selection criteria, and minimum standards for the informed consent process, including forms. This panel would include, among others, representatives of the artificial heart manufacturers, the hospitals involved in the artificial heart program, and the appropriate physicians. Please comment on this proposal.

3. It has been reported that you may become affiliated with the University of Louisville, and that if you were to do so, the University's IRB would routinely review your artificial heart implant protocols. In your opinion, what would be the advantages and disadvantages of such IRB review?

4. Have you submitted a revised implant protocol to FDA? If so, what action has FDA taken?

5. The major complication seen so far in all of your artificial heart recipients is strokes. Please describe the new ways you have devised for monitoring a patient's neurological condition.
   - Are you using these new procedures on Mr. Schroeder and Mr. Haydon, and if so, what have been the results?

6. Are Mr. Schroeder and Mr. Haydon still in need of frequent blood transfusions?

7. It has been suggested that a uniform master implant protocol be developed so that useful, consistent scientific information could be obtained from all the centers' use of a particular device. Please comment.

Your copy of the transcript, together with any written requests for changes, and your responses to the above questions should be returned by April 24, 1986 to:

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex I
Washington, DC 20515-6307

Your testimony at the hearing was extremely valuable to the Members, and I want to extend our thanks for your participation and service to the Subcommittee.

Sincerely,

Harold Volkmer
Harold L. Volkmer
Chairman
Subcommittee on Investigations
and Oversight

HLV/Gmbh

Humana
Heart Institute
International

May 5, 1986

Humana
Hospital
Audubon
One Audubon
Plaza Drive
Louisville, KY 40217
(502) 636-7135

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex 1
Washington, D.C. 20515-6307

Dear Dr. Glowinski:

Pursuant to the April 7, 1986, letter of Harold L. Volkmer, please find enclosed a copy of the transcript of the remarks at the February 5, 1986, hearing before the subcommittee on investigations and oversight.

Also, pursuant to Mr. Volkmer's request, following are responses to the questions posed in the April 7th letter.

1. A revised consent form was submitted to the Food and Drug Administration through Symbion, Inc. on April 2, 1986. Formal approval from the FDA has not yet been received, although it is expected shortly.

The consent form reflects information learned from experiences with the first four artificial heart recipients in a number of respects. First, the consent form incorporates information concerning the experiences of other artificial heart recipients so that prospective recipients may be fully informed concerning prior experiences. The consent form signed by Mr. Schroeder incorporated information concerning only the experiences of Barney Clark, as that was the only experience available at that time. The consent has further been amended to insert the term "experimental" in a number of additional places to emphasize that the artificial heart is experimental. There were revisions to the section of the consent form outlining possible complications to emphasize the possibility of strokes (which were already listed as among the complications in the previous consent form). In addition, the consent form now makes provision for a separate consent dealing with drugs which may be used in an experimental mode with artificial heart recipients.

The revised consent form makes no additional provision for alternative decision making should the patient become incompetent or unable to communicate.

In response to your third question, the Kentucky legislature failed to approve proposed legislation which would have allowed family members to participate in the decision making process. The proposed legislation was originally attached as an amendment to a "living will" bill which failed to pass. Thereafter, the legislation was separately proposed and also failed to pass.

2. The proposal for a "multi-center review panel" to be formed to develop uniform standards related to the artificial heart implant protocol and prosthesis is, in my view, superfluous in view of the already adequate review by the FDA and the Institutional Review Board at Humana Hospital-Audubon. It is the purpose of these bodies to review protocols, patient selection criteria and informed consent, among other factors. In addition, there are ongoing efforts to coordinate the various implant programs, including an International Conference on Cardiac Replacement, which was sponsored by Humana Hospital-Audubon, on April 23, 1986. Almost all of the physicians involved in implantation of artificial hearts on a temporary or permanent basis participated in that seminar. There have also been two (2) other meetings of principal investigators for the Jarvik heart to discuss problems, complications and protocols. There is, therefore, substantial scientific cooperation with respect to the artificial heart program. Development of yet another review panel with respect to this project would be both unnecessary and problematic for investigators who are already under scrutiny by a substantial number of organizations with adequate expertise at this time.

3. In response to your inquiry concerning my possible affiliation with the University of Louisville, I have been informed that the University's IRB would be desirous reviewing the artificial heart implant protocols. The advantages of such review would, of course, be the suggestions which could be forthcoming from an academic institution. However, as you know, the program at Humana Hospital-Audubon, and myself in particular, have been open to suggestions from all segments of the scientific community since the inception of the program and would continue to be receptive with or without formal IRB review by the University of Louisville. The disadvantages would involve the time required in submission to an additional review body and possible jurisdictional disputes should the University's IRB and the IRB of Humana Hospital-Audubon not agree with respect to some matter. It is my understanding, however, that any review by the University of Louisville IRB would be directed solely at the issue of my University appointment and would not affect review by the Humana Hospital-Audubon IRB, which is the authoritative body pursuant to the FDA regulations. At this point, the question of my appointment is not fully resolved.

4. A revised implant protocol was filed with the FDA on March 20, 1986, and was approved thirty (30) days thereafter.

5. Since we have had history of strokes, we have changed the intensity of therapy to prevent coagulation by increasing the dosages of drugs to prevent the blood from clotting, as well as adding other drugs to prevent the blood platelets from starting or adding to a clot. Both Mr. Schroeder and Mr. Haydon have been treated with the new protocol. Mr. Haydon has not had a stroke in twelve (12) months on the Total Artificial Heart and Mr. Schroeder has had no new neurological problems in over six (6) months.

6. Mr. Schroeder and Mr. Hayden are not in need of frequent blood transfusions.

7. With response to the suggestions that a master implant protocol be developed so that scientific information could be obtained from all the centers, note that I referred in paragraph number 2 to the very substantial sharing of information by and between the principal investigators. Among this group are some who preliminarily have expressed the view that a common protocol could be of value, while others feel it could be too restrictive. At this stage, it appears that the networking among principal investigators can serve a similar scientific function.

I hope these responses have been of assistance.

Sincerely,

Dr. William C. DeVries

WCD:jm

Enclosure

STATEMENT TO THE SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT OF THE COMMITTEE ON SCIENCE AND TECHNOLOGY, U.S. HOUSE OF REPRESENTATIVES

William C. DeVries, M.D.

February 5, 1986

MR. CHAIRMAN AND MEMBERS OF THE SUBCOMMITTEE:

I appreciate the opportunity to present the following comments and observations on the status of the artificial heart program. The interest of the subcommittee in having me testify is representative of the widespread interest throughout the country and the world in this program, and I am grateful yet a little mystifed that this scientific experiment has captured the imagination of such a large number of people. At the same time I am also troubled by some of the consequences of this interest. The necessity of dealing with outside scrutiny, whether from the news media, the Food and Drug Administration, colleagues or the general public, has taken valuable time away from the program -- both in terms of scientific inquiry and in terms of time spent with Bill Schroeder, Murray Haydon and their families. The other day a 3-year-old boy came up to me and said, "Didn't you used to be a doctor?" I had to nod my head because in truth that is only a slight exaggeration of the way I feel. I therefore welcome this forum as a chance to set forth my views at length and respond to questions, in hopes that the availability of these proceedings in printed form will enable me to be a doctor again.

The purpose of the artificial heart program is to develop a therapy that will be safe and effective in treating patients with end-stage heart disease. Coronary heart disease is this country's leading cause of death, and among its victims are many people for whom no known therapy -- including heart transplants -- is helpful. The number of these people is open to debate, but most estimates of how many heart patients could benefit from an artificial heart implant, if the procedure becomes an accepted therapeutic technique, fall in the range of 20,000 to 60,000 per year. A 1982 report submitted to the Congressional Office of Technology Assessment, for example, gave a mid-range estimate of 33,000 annually. Within this group are some people who would benefit from a ventricular assist device, a kind of helper-pump that is connected to a diseased heart. But many thousands of end-stage patients are afflicted with a heart that is too weak to benefit from ventricular support.

Under guidelines approved by the Food and Drug Administration, potential artificial heart recipients are strictly limited to patients who qualify as "Class IV" according to a system devised by the New York Heart Association. The classification states:

> Class IV patients have the inability to carry on any physical activity without discomfort. Symptoms of discomfort are present even at rest. With any physical activity, increased discomfort is experienced.

These guidelines further state that only Class IV patients for whom all appropriate therapeutic techniques have failed are eligible to receive an artificial heart. In practical terms this means that according to regulations, candidates for an artificial heart must be very close to death. Even use of the artificial heart as a bridge to transplant must be for patients in a life-threatening situation. The artificial heart is therefore a last resort.

The current status of the artificial heart program can be summarized as follows: it is an ongoing experiment which, after more than 25 years of planning, laboratory development and testing on animals, has progressed to the clinical investigation stage. Five different Total Artificial Hearts (TAH) -- to distinguish from Ventricular Assist Devices (VAD) -- have so far received clinical trials (see Table 1). At Humana Heart Institute International, where I am principal investigator for the TAH, the heart under investigation is the JARVIK-7, manufactured by Symbion, Inc., of Salt Lake City, Utah. In its FDA-approved form (1), the JARVIK-7 is a plastic-and-metal, air-driven pump, connected by two drive lines above the abdomen to one of two external power sources -- a semi-stationary unit called the UTAHDRIVE, or the portable HEIMES driver. I am using this heart because I think it is the best one currently available. If a better heart is developed -- by Symbion or anyone else -- I would use it, as long as it has the

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(1) A smaller version of the JARVIK-7 has been implanted in one patient in Minneapolis, Minn., but does not have FDA approval.

TABLE 1

TOTAL ARTIFICIAL HEARTS IMPLANTED

TX = heart transplant

PATIENT	AGE	LOCATION	DATE	SURGEON	HEART TYPE	COMPLICATIONS	OUTCOME
HK	47	Houston, Tx.	04-04-69	Cooley	Liotta	Unconscious Bleeding	TAH-64 hrs Tx-3 hrs Died
RM	32	Houston, Tx.	07-23-81	Cooley	Akutsu	Unconscious Bleeding	TAH-47 hrs Tx-8 days Died
BC	61	Salt Lake City, Utah	12-02-82	DeVries	Jarvik-7	Bleeding Seizure Renal failure	TAH-112 days Died
BS	53	Louisville, Ky.	11-25-84	DeVries	Jarvik-7	Bleeding Stroke x 3	TAH-14 months Alive
MH	59	Louisville, Ky.	02-17-85	DeVries	Jarvik-7	Bleeding Stroke x 1	TAH-11 months Alive
JB	63	Louisville, Ky.	04-15-85	DeVries	Jarvik-7	Bleeding Renal failure	TAH-10 days Died
LS	54	Stockholm, Sweden	04-07-85	Semb	Jarvik-7	Bleeding Stroke x 2	TAH-9 months Died
RL	34	Tucson, Az.	03-06-85	Copeland	Phoenix	Renal failure	TAH-11 hours Tx-2 days Died
MD	26	Tucson, Az.	08-29-85	Copeland	Jarvik-7	Stroke	TAH-9 days Tx-Alive
AM	44	Hershey, Pa.	10-18-85	Pierce	Penn State	Multi-organ failure	TAH-10 days Tx-16 days Died
TG	47	Pittsburgh, Pa.	10-24-85	Griffith	Jarvik-7	Bleeding	TAH-5 days Tx-Alive
ML	40	Minneapolis, Minn.	12-18-85	Joyce	Jarvik-7-70	Bleeding Renal failure Neurological problems	TAH-45 days Tx-Alive

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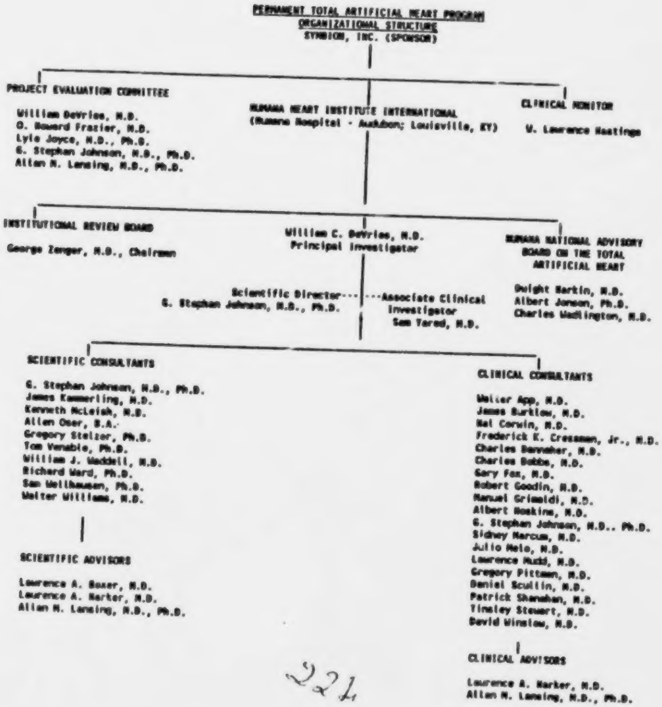
approval of the FDA and the Institutional Review Board of the hospital where the experiment is taking place. It is worth noting, however, that the dream of everyone involved with the artificial heart is to one day perfect a totally implantable device that would enable a recipient to live a life as normal as yours or mine. The JARVIK-7, like the other hearts under investigation, is a necessary step on the road to the achievement of this dream. It will never be realized unless these interim hearts are clinically evaluated and their effect on patients thoroughly examined. As with all useful inventions, the artificial heart must pass through the refiner's fire of testing.

Humana Heart Institute International is located at Humana Hospital - Audubon in Louisville, Kentucky, where I am also engaged in the private practice of cardiovascular surgery. I do not receive a salary, stipend or any other remuneration for my work on the artificial heart program from the Heart Institute or Humana Inc. My work on the project, and that of my medical and surgical colleagues, as well as that of many devoted clinical and scientific advisors, is done gratis. I say this to set the record straight on a point that has given rise to much speculation. Humana's role in the project is to provide the clinical setting and to meet the hospitalization costs of artificial heart recipients. The company's corporate staff has never sought to influence my conduct of the project, and Humana neither owns nor seeks patent, copyright, or any other legal protection for the techniques and materials I am using. I have made a point of sharing what I have learne with Dr. Jack Copeland in Tucson, Dr. Lyle Joyce in Minneapolis, Dr. Bjarne Semb in Stockholm and many others involved with the clinical development of the artificial heart, and have been encouraged by Humana in this effort. Its status as a "for-profit" health care corporation has not caused me to change the way I work on the artificial heart. I worked on it for 18 years before I came to a Humana hospital a year and a half ago, and I am confident that the habits I developed over that period of time will remain unaffected by the tax-paying status of whatever clinical setting I practice in. That does not answer the question of why Humana agreed to fund as many as 100 implants, as long as scientific progress continues to be made, but it's not for me to answer. They never asked me why I agreed to devote my life to the project. I do know that the common ground between us is a desire to give suffering people the best possible medical care. David A. Jones, Humana's chief executive officer, explains it this way: "There's nothing in it we can gain other than a reputation for having a high quality hospital where even the most sophisticated and difficult procedures can be safely performed." Having worked intensely with the Institute staff I can assure you they have been up to the special demands of clinical research and were at least as well prepared for the implants at Audubon as the staff at the University of Utah was for the Barney Clark implant in 1982.

Along with FDA reporting requirements, which have recently been expanded, the artificial heart program at Humana Heart Institute International is monitored by several on-site and off-site groups, as well as by clinical, scientific and ethical consultants from throughout the United States (see Table 2). The input of many dedicated professionals ensures that the project is proceeding according to the highest scientific standards; their expertise is also useful in an

TABLE 2



PERMANENT TOTAL ARTIFICIAL HEART PROGRAM
ORGANIZATIONAL STRUCTURE
SYMBION, INC. (SPONSOR)

PROJECT EVALUATION COMMITTEE

William DeVries, M.D.
O. Howard Frazier, M.D.
Lyle Joyce, M.D., Ph.D.
G. Stephan Johnson, M.D., Ph.D.
Allan M. Lansing, M.D., Ph.D.

HUMANA HEART INSTITUTE INTERNATIONAL
(Humana Hospital - Audubon; Louisville, KY)

CLINICAL MONITOR

V. Lawrence Hastings

INSTITUTIONAL REVIEW BOARD

George Zenger, M.D., Chairman

William C. DeVries, M.D.
Principal Investigator

HUMANA NATIONAL ADVISORY
BOARD ON THE TOTAL
ARTIFICIAL HEART

Dwight Harkin, M.D.
Albert Jonson, Ph.D.
Charles Wadlington, M.D.

Scientific Director
G. Stephan Johnson, M.D., Ph.D.

Associate Clinical
Investigator
Sam Tared, M.D.

SCIENTIFIC CONSULTANTS

G. Stephan Johnson, M.D., Ph.D.
James Kammerling, M.D.
Kenneth McLeish, M.D.
Allen Oser, B.A.
Gregory Stelzer, Ph.D.
Tom Venable, Ph.D.
William J. Waddell, M.D.
Richard Ward, Ph.D.
Sam Wellhausen, Ph.D.
Walter Williams, M.D.

SCIENTIFIC ADVISORS

Lawrence A. Boxer, M.D.
Laurence A. Harker, M.D.
Allan M. Lansing, M.D., Ph.D.

CLINICAL CONSULTANTS

Walter App, M.D.
James Burklow, M.D.
Mel Corwin, M.D.
Frederick K. Cressman, Jr., M.D.
Charles Bennaher, M.D.
Charles Dobbs, M.D.
Gary Fox, M.D.
Robert Goodin, M.D.
Manuel Grimaldi, M.D.
Albert Hoskins, M.D.
G. Stephan Johnson, M.D., Ph.D.
Sidney Marcum, M.D.
Julio Melo, M.D.
Lawrence Mudd, M.D.
Gregory Pittman, M.D.
Daniel Scullin, M.D.
Patrick Shanahan, M.D.
Tinsley Stewart, M.D.
David Winslow, M.D.

CLINICAL ADVISORS

Laurence A. Harker, M.D.
Allan M. Lansing, M.D., Ph.D.

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advisory capacity. I draw your attention especially to the distinguished group of scientific consultants and scientific advisors -- panels one rarely finds in an academic research setting. The following pages provide a summary of their responsibilities.

ORGANIZATIONAL STRUCTURE AND PERSONNEL

A. Sponsor: Symbion, Inc.

B. Clinical Monitor: Larry Hastings - Symbion, Inc.

C. Project Evaluation Committee:

1. Members
William DeVries, M.D. - Humana Heart Institute International
O. Howard Frazier, M.D. - Texas Heart Institute
Lyle Joyce, M.D. - Minnesota Heart Institute
G. Stephan Johnson, M.D., Ph.D. - Humana Hospital - Audubon
Allan M. Lansing, M.D., Ph.D.
Humana Heart
Institute International

2. Responsibilities:

To evaluate the clinical data and provide advice to Symbion regarding modifications and development of the clinical protocol.

D. Principal Investigator: William C. DeVries, M.D.

E. Institutional Review Board, Humana Hospital - Audubon:
George Zenger, M.D., Chairman

F. Humana National Advisory Board on the Total Artificial Heart Project:

1. Members:
Dwight Harkin, M.D. - Harvard University
Albert Jonsen, Ph.D. - University of California at San Francisco
Charles Wadlington, M.D. - University of Virginia

2. Responsibilities:
To advise Humana, Inc., on the following issues concerning the Total Artificial Heart Project:

(a) Review the artificial heart implant protocol and the related informed consent document, offering suggested improvements in legal, ethical, scientific or other areas.

(b) Review the makeup and performance of the Institutional Review Board of Humana Hospital - Audubon, offering suggestions for improvement in any area, including the possibility of broadening its membership.

(c) Review the issue of patient privacy versus public and scientific need for knowledge, including the development of policies and procedures which assure full and timely dissemination of knowledge gained and results achieved in this experimental program.

(d) Review the steps taken by Humana, Inc., to guarantee financial support and clinical independence of this program, offering appropriate suggestions for improvement.

(e) Identify other areas which should be considered by Humana, Inc., not already addressed by the FDA regulations and the medical investigators in this research, offering suggestions on how to deal with any such activities.

G. Scientific Director: George S. Johnson, M.D., Ph.D.

1. Responsibilities:

(a) To coordinate the preparation, review, and implementation of scientific protocols.

(b) To supervise data collection, analysis, and storage.

(c) To provide quarterly reports to Symbion for submission to FDA.

(d) To facilitate scientific publications.

H. Associate Clinical Investigator:

(1) Sam Yared, M.D.

(2) Responsibilities: to assist Dr. DeVries and to coordinate patient clinical support.

I. Scientific Consultants: These scientists or clinicians provide the necessary scientific support to the permanent artificial heart clinical investigation. None, except as indicated below, are employed by Humana, Inc.

- Johnson, George S., M.D., Ph.D.*
  - Pathology/Laboratory Medicine, HHII[+]
- Kammerling, James, M.D.
  - Hemodynamics; Cardiac Physiology, HHII[+]
- McLeish, Kenneth, M.D.***
  - Nephrology, University of Louisville
- Oser, Allen, B.A.**
  - Data Collection, Humana, Inc.
- Stelzer, Gregory, Ph.D.***
  - Immunology, University of Louisville
- Venable, Tom, Ph.D.**
  - Biostatistics, Humana, Inc.
- Waddell, William J., M.D.***
  - Pharmacology, University of Louisville
- Ward, Richard, Ph.D.***
  - Engineering, University of Louisville
- Wellhausen, Sam, Ph.D.***
  - Immunology, University of Louisville
- Williams, Walter, M.D.***
  - Pharmacology, University of Louisville

*As the Scientific Director for the Permanent Total Artificial Heart study, Dr. Johnson will be employed half-time by Humana, In

**Full-time Humana, Inc. employee.

***These scientists have full-time faculty appointments at the Univer sity of Louisville and will consult with the Humana Heart Institut International on a daily basis as necessary.

[+] Humana Heart Institute, International

J. **Clinical Consultants**: These scientists and clinicians have staff appointments, but they are not employed directly by Humana, Inc. At Humana Hospital - Audubon, they provide scientific and clinical support to the permanent artificial heart clinical investigation.

Anesthesiology -	Shanahan, Patrick, M.D.
Cardiology -	Goodin, Robert, M.D.*
Hematology -	Dobbs, Charles, M.D.*
	Grimaldi, Manuel, M.D.*
	Scullin, Daniel, M.D.*
	Dannaher, Charles, M.D.
Internal Medicine -	Hoskins, Albert, M.D.*
Immunology -	Burklow, James, M.D.
Infectious Disease -	Melo, Julio, M.D.*
Nephrology -	Marcum, Sidney, M.D.*
	Woo, Daniel, M.D.*
Neurology -	Fox, Gary, M.D.*
	Corwin, Hal, M.D.
	Pittman, Gregory, M.D.
	Stewart, Tinsley, M.D.
Pathology/Laboratory -	Cressman, Frederick K., Jr., M.D.*
	Johnson, G.Stephan, M.D., Ph.D.*
Psychiatry -	Mudd, Lawrence, M.D.
Pulmonary Medicine -	Winslow, David, M.D.*
	App, Walter, M.D.*

Please note the letters of committment/curriculum vitaes of the aforementioned scientific and clinical advisors and consultants are contained in Appendix E.

*These individuals also hold clinical staff appointments at the University of Louisville.

K. **Scientific Advisors**: Experts who provide advice to Humana Heart Institute International concerning the scientific protocols:

Boxer, Lawrence A., M.D. - Hematology, University of Michigan
Harker, Laurence, M.D. - Hemostasis/Thrombosis, Scripps Clinic
Lansing, Allan M., M.D., Ph.D. - Cardiac Physiology/ Cardiovascular Surgery, Humana Heart Institute International

L. **Clinical Advisors**: Experts who provide advice to Humana Heart Institute International concerning the clinical protocols:

Harker, Laurence, M.D. - Hemostasis/Thrombosis, Scripps Clinic
Lansing, Allan M., M.D. - Cardiovascular Surgeon, Humana Heart Institute International

M. Nursing:

Davis, Pat, R.N. - Nursing Coordinator
Boyer, Martha, R.N., - Co-Nursing Coordinator
Wood, Laura, R.N. - Inpatient Services
Shaheen, Kevan, R.N. - Outpatient Services
Marsh, Linda, R.N. - Operating Room

M. Ancillary Services:

1. Laboratory Services:

Fisher, Carolyn, MT (ASCP), SC, M.A.
Burke, Gail, MT (ASCP), SBB, B.S.

2. Respiratory Therapy:

Wendell, Leo, ARRT

3. Physical Therapy:

Schaefer, Joan, PT

4. Social Services:

Rhine, Gary, MSSW

5. Occupational Therapy:

Duncan, Sandy, O.T.R.

6. Dietary:

Guynes, Pam, R.D.
VonDreele, Marion, R.N.

O. Drive System Management:

Barker, Lawrence, R.N.
Mays, Brent, P.A.-C.
Williams, Melissa, P.A.-C.

P. Data Management

Venable, Tom, Ph.D. - Biostatistics
Oser, Allen, B.A. - Data Collection

Artificial heart recipients fall into two groups: permanent and temporary. Patients may go from one group to another as medical indications change. Of the four implants I have performed, all have been permanent. The first was done at the University of Utah on December 1, 1982; the patient was Barney Clark, who lived 112 days. Implant patients at Humana Heart Institute International have been William Schroeder (November 25, 1984; living after 438 days), Murray Haydon (February 17, 1985; living after 354 days) and Jack Burcham (April 14, 1985; died after 10 days).

When these results are compared with other medical experiments at a similar investigational stage, they are incredible. Based on length of life the artificial heart is an astonishing scientific achievement. By way of comparison, 100 patients received a human heart transplant in the year after Dr. Christaan Barnard pioneered the technique. Only 17 were still alive at the end of that year (December, 1968). Causes of death included stroke, kidney failure, brain damage, pulmonary embolism, heart failure, rejection, multiple systemic complication and cerebral-vascular accident (2). The first 15 patients to undergo kidney dialysis died within hours or days; the 16th patient's life was saved. Patient survival following liver transplantation, an approved therapeutic technique, is still only 65 percent at the end of the first year -- and even that represents an increase of 100 percent above the level of five years ago. The long survival rate of the first artificial heart recipients gains added signifiance when their nearness to death at the time of implantation is recalled.

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(2) Haller, J.D. and Cerruti, M.M., "Heart Transplantation in Man." American Journal of Cardiology, Oct. 1969, pp. 554-563.

I have FDA approval to perform three more implants, provided I adhere to the new reporting procedures. These measures require me to submit reports every three months on each patient receiving the JARVIK-7 as a permanent replacement heart. In addition, the FDA must now give advance approval for each new permanent implant, based on their interpretation of the success of the previous one.

My experience with permanent implants does not mean I am opposed to the use of the artificial heart as a bridge to a human heart transplant. Each potential candidate is evaluated independently, and if medical judgment deems temporary use appropriate, I look forward to trying it. As an investigator I must add, however, that a bridge to transplant provides a much less adequate assessment of the artificial heart's strengths and weaknesses than a permanent implant. In bridge operations the patient's welfare is not just paramount, as it is in any implant, but exclusive. The artificial heart is seen not as potential therapy in itself, but as a stepping-stone toward the real therapy -- a transplant. Study of the artificial heart's performance is therefore necessarily minimized as the physician concentrates all his energies on keeping the patient alive and comfortable until a transplant can be performed. With permanent implantation, the heart's interaction with the blood, lungs, kidneys, liver and other organs is of the first importance. Data is closely monitored and changes (such as regulation of the heart rate) are made with the goal of accommodating the heart as part of the patient's long-term well-being. In addition, experience has shown that many of the artificial heart's complications do not become apparent in the normal time-frame of the bridge to transplant. Ultimately, an adequate determination of the artificial heart's therapeutic potential will depend on the data that only an extensive series of permanent implants can provide.

Patient Selection Criteria

Potential recipients of a JARVIK-7 artificial heart at Humana Heart Institute International are referred either by themselves, their cardiologist or local physician. If the patients are referred by themselves, their physician is contacted and the patient's clinical summaries, laboratory determinations, diagnoses and hospital records are sent from the physician. Patients are initally screened by me and those with obvious difficulties, such as certain pre-existent diseases, are ruled out. If the patient appears to be a satisfactory candidate, he is admitted to Humana Hospital - Audubon, where he is evaluated by the heart transplant specialists for possible heart transplantation. If the patient is rejected for transplant, artificial heart laboratory workups are undertaken. The patient is then considered by the clinical consultants and the evaluation committee. If the evaluation committee approves the candidate, I meet with him and his family to discuss the contents of the Special Patient Consent form. A copy of this form follows.

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SPECIAL PATIENT CONSENT FOR THE IMPLANTATION OF THE TOTAL ARTIFICIAL HEART AND RELATED PROCEDURES

1.0 I, the undersigned, understand that on the basis of various diagnostic procedures, it has been determined that I have a condition known as: ____

____
(describe condition)

which has so seriously impaired the function of my heart that I have been placed in category IV of the New York Heart Association classification of heart disease, which states:

> Class IV patients have the inability to carry on any physical activity without discomfort. Symptoms of discomfort are present even at rest. With any physical activity, increased discomfort is experienced.

It is the judgment of physicians and others who have evaluated my diagnostic tests that, although no specific life span can be estimated, it is probable that I will die much sooner than most others of my age and that while alive I will continue to be severely restricted due to my failing heart. I also understand that it is highly likely that further medical therapies will not arrest the course of my deteriorating heart condition. While it has not been proven in humans that a Total Artificial Heart will prolong my life beyond that which is expected for my condition I am willing to submit to the implantation of the Total Artificial Heart on an experimental basis in order to determine if it will help other people with this condition, and for the possible beneficial affects that I may obtain from the experiment.

1.1 Any consideration as to my selection for a natural heart transplant procedure in the future requires a determination by an independent cardiac transplantation team. I understand that it is most probable that a Total Artificial Heart will be the final alternative as a life-sustaining device. However, I understand that I may not qualify for and that no assurances have been made to me regarding my selection for a natural heart transplant.

2.0 I recognize that the ventricles (the larger two of the heart's four pumping chambers) from my own natural heart will be removed and a Total Artificial Heart will be placed within my chest in the space formerly occupied by my own ventricles. This mechanical device will require my body to be attached to an air-drive system by two plastic air tubes to pump my blood through my mechanical heart and circulate it through my body. I am aware that my life style will be significantly different with a Total Artificial Heart. My activity will be severely limited because of the drive lines and I will be dependent upon an external air-drive system to power the Total Artificial Heart. The external drive systems may not necessarily require me to be bedridden but at best would allow me to move from room to room, and may allow brief periods of being outdoors and riding in a car or van if it is capable of carrying the external drive system. I may be able to carry on many life functions in a normal manner (e.g., toilet activity, eating, reading, and desk work). It is possible, however, that I may be bedridden due to pain, weakness, or other problems.

2.1 I further understand that in addition to the primary implantation surgery of a Total Artificial Heart additional chest surgeries may be required for repair or adjusting of the Artificial Heart, the air drive lines or other related structures. In the event such corrective surgeries are required, these procedures will be explained to me and my consent will be required for each such procedure. General anesthesia with its attendant risks may be necessary in connection with such procedures.

2.2 In the event my physician determines that I am too sick because of my physical or mental condition to understand the nature of such repair(s) or adjustment(s) and the required corrective surgery(ies), or to execute such additional Consent(s), I hereby authorize, empower, and direct either ______________________ or ______________________ to act in my behalf. (Such person must be over eighteen years of age. Designate relationship, if any.)

2.3 I also understand that if a Total Artificial Heart is implanted I can anticipate considerable postoperative pain and discomfort similar to or greater than that which would be experienced following the usual type of cardiovascular surgery, and that additional or prolonged discomfort and pain may result in the event of further surgery. If in connection with the implantation of the Total Artificial Heart my physician, in his judgment, determines that additional instrumentation and studies may advance medical science or benefit me, then he is authorized to undertake the same. Before such studies are undertaken, their processes and risks will be explained to me to my satisfaction. Such studies may include the use of different forms of heart drivers in order to determine if my mobility may be increased, or to develop a more effective driving system(s).

3.0 I recognize that during the course of the implantation of the Total Artificial Heart or subsequent surgeries and procedures, unforseen conditions may necessitate additional or different procedures than those set forth in Section 2 above. In such event I authorize my physician to perform such procedures as are, in his professional judgment, necessary and desirable. The authority granted under this Section 3, shall extend to attempts to treat or remedy any condition(s) that are not known at the time the surgery or procedure is undertaken.

4.0 I consent to the administration of anesthesia as arranged by my physician with such assistants as may be designated, and to the use of such anesthetics as they deem advisable.

5.0 I have also been informed of the substantial risks involved in cardiovascular surgery and the administration of general anesthesia, and understand that there are additional risks beyond those normally associated with cardiovascular surgery, as a result of a Total Artificial Heart implantation, which may result in serious bodily impairment, or death. These risks include:

(a) Emboli or blood clots which may lead to stroke, kidney loss, liver, bowel or lung dysfunction, or damage to other organs or body functions.
(b) Malfunction or mechanical failure of the Total Artificial Heart device or breakage of the Total Artificial Heart valves.

(c) Infection of:
  (1) My blood (sepsis),
  (2) The drive lines to the Total Artificial Heart device, or
  (3) Within the Total Artificial Heart itself.

(d) Hemorrage resulting from:
  (1) The action of the Total Artificial Heart upon the vessels,
  (2) Surgery to expose the natural heart,
  (3) Deficiencies in the blood clotting mechanisms secondary to the Total Artificial Heart,
  (4) Anticoagulation medication.

(e) Damage to:
  (1) The red blood cells (that carry oxygen and carbon dioxide),
  (2) The platelets (that cause blood to clot),
  (3) White blood cells (that act as scavengers against foreign substances and provide for immunization) which might cause a change in my blood immune system or anemia.

(f) Pneumothorax (air in the chest cavity from my lungs or as a result of leakage from the Total Artificial Heart itself). This may result in breathing difficulties requiring a separate tube(s) to be placed in my chest, or an operation to treat the defect.

(g) Seizures or convulsions due to emboli, metabolic imbalance or blood flow imbalances from the Total Artificial Heart placed in my chest.

(h) Renal failure or inability of my kidneys to excrete metabolic waste products or fluids.

(i) Pulmonary insufficiency causing shortness of breath or necessitating prolonged respirator support.

Because this is a highly experimental procedure other unforseeable risks may arise, and the above listed potential problems should be considered only as illustrative, and not all inclusive.

6.0 I further recognize that this procedure is experimental. Similar Total Artificial Heart devices have been implanted in two patients in other institutions as temporary emergency, life-prolonging procedures until heart transplants could be obtained. The devices used in these patients were not the model of the Total Artificial Heart which will be used in my case. With these two patients the artificial heart was removed and a heart transplant performed, and both of these patients died within one week from complications.

6.1 On December 1, 1982, a 61-year old dentist, Dr. Barney Clark, had his failing natural heart removed and a Total Artificial Heart implanted. His Total Artificial Heart was similar to the one that I will have implanted in me, except that the heart valves are a different type. Dr. Clark lived for 112 days in the University of Utah Hospital until his death which resulted from infection. During his life with the Total Artificial Heart, Dr. Clark experienced kidney and lung problems, a pneumothorax (air in the lung cavity), valve breakage, seizures, bleeding complications and depression. He remained hospitalized during the entire 112-day period. The medical team at the Humana Hospital-Audubon have thoroughly discussed Dr. Clark's case with me and have answered all of my questions concerning the case to my satisfaction.

6.2 The University of Utah has had considerable experience with living animals implanted with a similar model of a Total Artificial Heart as will be used in my case. The present human model has had only limited testing in these animals. However, the device to be used is believed to be the most refined and advanced model which is available for use in a human at this time. To date the longest an animal (a ram) has lived with a Total Artificial Heart is approximately nine months (297 days). Most animals lived for approximately three months and the majority died from infections caused by bacteria entering around the drive tubes or other tubes used to monitor the function of the heart. Other common causes of death in these animals were: infected blood obtained from packing houses which was used in transfusions, insufficient blood volume being pumped through the heart as the animals grew, and the mechanical problems which developed with the Total Artificial Heart. While these complications may be due to problems which may be unique to animal experimentation, they may also provide warnings of risks, which should also be considered in addition to other potential complications outlined in this document.

7.0 No representations or guarantees have been made to me either that the procedure will be successful, or the length of time or the level at which the Total Artificial Heart will function. Nor have any guarantees or assurances been made to me that the implantation of the Total Artificial Heart will add any additional time to my life expectancy. In fact, I understand this implantation may shorten my life and/or reduce the quality of my remaining life. I recognize that if the Total Artificial Heart fails, death or serious illness is the near certain result. I nevertheless accept the risks of substantial and serious harm, including death, in the hope that the beneficial effects of the implantation of the Total Artificial Heart can be demonstrated, and that scientific information may be obtained which may be useful to others or myself.

8.0 I acknowledge that my physician has satisfactorily explained to me the procedure involved in the implantation of the Total Artificial Heart and that all my questions about the procedure and its attendant risks, including death, the experimental nature of the Total Artificial Heart, its expected function, and the probability of continued hospitalization and medical care, have been fully answered to my satisfication.

9.0 I have been informed that in several medical centers cardiac assist pumps are under development. My physician has satisfactorily explained to me the development, status, use, function, risks and availability of such cardiac assist pumps and has answered all my questions concerning such devices.

10.0 I recognize that following surgery I may require extended hospitalization and/or further treatment, including further surgery.

11.0 I hereby authorize Humana Hospital-Audubon through its authorized agents to dispose of or use for medical or scientific purposes, any tissue or body parts which may be removed during the surgical procedures and/or autopsy.

12.0 For the purpose of advancing medical knowledge, I authorize and consent to the presence of medical students and other professional medical observers, during my surgery(ies) and other medical procedures. I also authorize and consent to the use of video taping through closed circuit television, the taking of photographs (including motion pictures), the preparation of drawings and similar illustrative graphic material, and to the use of these graphic materials for scientific purposes. I acknowledge that the U.S. Food and Drug Administration will have access to the data from this experiment and that they will make no public use of these materials for purposes other than scientific presentation, except as may be required by law.

13.0 I am fully aware of the considerable public interest anticipated in my story as a recipient of a Total Artificial Heart. I am also aware that the Humana Hospital-Audubon has an obligation to disseminate medical information concerning my hospital course as deemed appropriate in the judgment of my physician. In addition to those materials identified in paragraph 12, the Humana Hospital-Audubon, as approved by my physician, is authorized to make, or permit to be made, photographs, slides, films, video tapes, recordings or other means of recording and/or communicating hereinafter referred to as "material(s)," that may be used in newspaper, magazine articles, television, radio broadcasts, movies or any other media or means of dissemination. I consent to the use of my name, likeness, or voice for such purposes and I release the Humana Heart Institute, Humana Hospital-Audubon, their officers, agents, and employees from all claims of liability with respect to the showing, use or dissemination of such material(s). I understand that the materials which are made public, as described in this paragraph, will protect my modesty and be within generally accepted bounds of good taste.

14.0 I have also reviewed with my physician, and those with whom I live, the considerable financial obligations including costs of surgery, hospitalization, continuing instrumentation, studies and monitoring that living with a Total Artificial Heart will impose upon me. I understand that I am responsible for such costs to the extent that I may have insurance or other third party payment plans that will pay for such costs. Humana Hospital-Audubon will assume and pay the following costs, and none other, relating to this experiment which shall extend through my hospitalization and post-hospitalization period, to the extent not paid by insurance or third-party payment plans:

(a) Medical services of physicians and support staff,
(b) Equipment, maintenance and medical supplies related to the Total Artificial Heart,
(c) Hospital care,
(d) Diagnostic services,
(e) Reasonable long-term or extended medical care as determined by my physician,
(f) Such other costs as my physician in his sole discretion shall determine. In the event of dispute as to whether a particular cost is to be paid by Humana Hospital-Audubon the decision of my physician, Dr. William C. DeVries, shall be final.

15.0 I understand that by signing this document I do not acquire any right to a Total Artificial Heart implantation. I further understand that subsequent to my signing this form I could be deemed not acceptable to receive an implantation of a Total Artifical Heart for any reason whatsoever, including, but not limited to, physiological or medical considerations.

15.1 I also realize that the available Total Artificial Heart may not be implanted if it is believed to be malfunctioning, if a crucial member of the surgical team is unavailable at the time surgery is scheduled, if my condition changes (for either the better or for the worse), or if complications are experienced during surgery, but within these limitations all decisions will be based on reasonable medical judgment.

15.2 In the event the Total Artificial Heart, or any parts thereof are removed from my body, Humana Hospital-Audubon shall have the exclusive right to possession and control of the same, and that upon my death I consent to the removal from my body of the Total Artificial Heart.

16.0 I understand that Dr. William C. DeVries, or any other member of the Total Artificial Heart Evaluation Committee named below may determine in their sole discretion, that implantation is not appropriate and the Total Artificial Heart will not be implanted. The Evaluation Committee as identified below must be unanimous in its decision to implant a Total Artificial Heart.

(Name) (Title) (Position on Committee)

1. ____
2. ____
3. ____
4. ____
5. ____
6. ____

17.0 I understand I am free at any time to withdraw my consent to participate in this experimental project at any time prior to implantation of a Total Artificial Heart, thereafter I reserve the right to discontinue additional participation in experimental procedures, in which event supportive care will be continued on my behalf.

18.0 The provisions of this Special Consent shall be binding upon my heirs, assigns and personal representatives, and shall be construed in accordance with the laws of the Commonwealth of Kentucky.

19.0 I have discussed all reasonable alternative treatments with my physician including the possibility of no treatment, further drug treatment, attempts at possible surgical repair of my own failing heart, and natural heart transplants. After having these alternatives and their probable effects on my case explained to me, and with all of the considerations in mind as outlined above, and with the further understanding and recognition of the risks and the additional matters set forth in this document, I hereby request and authorize Dr. William C. DeVries, who is referred to in this Special Consent as "my physician," and such assistants and associates as he may designate, to proceed with the implantation of an experimental Total Artificial Heart in place of ventricles of my diseased natural heart.

20.0 This Special Consent contemplates that after I sign the same a 24-hour period will elapse before affixing any signature a second time pursuant to paragraph 22. However, if, in the opinion of my physician my physical condition begins to deteriorate in such a manner that there is substantial risk that I may die before the 24-hour period elapses, my physician is authorized to proceed with the implantation of the Total Artificial Heart. I understand that neither the waiting period nor my second signature is necessary for this Consent to be fully effective.

21.0 I acknowledge by my signature to this Special Consent that I have read and understand the foregoing, including the risks involved, that all questions pertaining thereto have been fully answered to my satisfaction, and that I have signed the same as my own free act and deed.

Dated at Louisville, Kentucky, this __________ day of _________________, 19__, at _____ o'clock _____.m.

____
(Patient's signature)

Witness:

____

_________________________________ M.D.
(Signature of physician)

22. I acknowledge that I have signed the foregoing Special Consent at least 24 hours previously, and have since had the opportunity to further consider the risks of the procedure. After such additional consideration, it is still my desire to have my physician proceed with the implantation of a Total Artificial Heart, and I hereby confirm and ratify this Special Consent and all provisions thereof.

Dated this _____ day of _________________, 19__ at ______o'clock __.m.

____
(Patient's signature)

Witness:

____

_________________________________M.D.
(Signature of physician)

If you have any questions regarding this experiment you may contact Dr. William DeVries at 636-7135 or 584-6413 after 5:00 p.m. or on weekends.

The patient is free, of course, to decline participation, without prejudice to his course of treatment. Some of my patients have declined. In the case of patients who cannot come off of a heart-lung machine (i.e. patients who will die without successful surgical intervention), or for emergency procedures, the foregoing process does not apply. Adequate protocols have been developed for patients unable to be disconnected from a heart-lung machine. Emergency procedures are complicated and appropriate protocols are being worked out.

Summary of What Has Been Learned Through Clinical Experience To Date

Clinical experience with the artificial heart has yielded a gold mine of scientific information. Not only have we at the Heart Institute modified our procedures to the benefit of future artificial heart recipients, based on the results of four permanent implants, but data in some areas open the exciting prospect of "spinoff" advances for related areas of medicine. In addition, the program's contribution to public awareness and education, mainly through media coverage, is of incalculable benefit. I think the average American is better informed today about heart disease and its risk factors, organ donation and a variety of related issues as a result of the artificial heart project than he was before it began.

Our experience in coping with neurological problems suffered by William Schroeder and Murray Haydon suggests ways of reducing the potential for strokes in high-risk patients. The necessity of balancing the use of anti-coagulation drugs, to minimize strokes, against the danger of internal bleeding if the blood is too thin, led us to develop principles with general application to cardiac surgery. Mr. Schroeder's valiant rallies from three strokes point not only to his own astonishing courage and perseverance, but also to our success in developing rehabilitative techniques. In the field of hemodynamics, we have changed the UTAHDRIVE system to give a "softer" pumping action, thus drastically reducing hemolysis (destruction of red blood cells) in Mr. Schroeder and Mr. Haydon. As a result their need for risky and debilitating blood transfusions, which contributed significantly to episodes of renal failure, has almost disappeared. Finally, we have gained important new insights into immunosuppression that suggest application to the general study of how the body fights infectious diseases. Mechanical circulatory assistance is an important future therapeutic reality, whether in the form of Total Artificial Hearts, Ventricular Assist Devices or yet-to-be-developed technologies. Studies of patients with the artificial heart benefit all scientists and physicians engaged in studying the contact of blood with foreign objects.

1. STROKES: PREDICTION AND MONITORING

The strokes suffered by Mr. Schroeder (three) and Mr. Haydon (one, with no lasting effects) have given rise to protocol changes designed to reduce the risk of neurological events and to deal more effectively with them if they occur. These modifications have application to anyone considered susceptible to strokes. It should be noted that animal studies give little hint of possible neurological problems with the artificial heart because of fundamental differences in human and animal brain circulatory systems, and because only 7 per cent of an animal's heart stroke volume goes to the brain. (In human beings the figure is 25 percent.)

Mr. Schroeder had preoperative neurologic testing including a CT brain scan and EEG. Murray Haydon and Jack Burcham had complete neurological histories and physical evaluations prior to surgery, as well as CT brain scans, EEGs and carotid ultrasound studies. For future patients, the preoperative evaluation will consist of the above, except that cerebral arteriograms will be substituted for carotid ultrasound studies. The purpose of the preoperative cerebral arteriograms is to examine the intracranial circulation in great detail and to evaluate the carotid arteries more precisely. The study will provide a sensitive baseline for thromboembolic events as well as a means of eliminating patients with severe cerebral arteriosclerotic involvement who are not appropriate candidates for implantation.

Postoperatively, patients will be monitored from a neurological standpoint at least every other day for the first two weeks and then twice a week. An EEG will be obtained during the first postoperative week and on a monthly basis thereafter. A CT brain scan will be taken at the end of a month and then every three months; cerebral arteriograms will be made two months after the operation and four to six months thereafter. The effect of these tests will be to detect early warning signs of a possible stroke.

2. STROKES: THROMBUS FORMATION IN THE ARTIFICIAL HEART

As mentioned earlier, experience with all artificial heart patients has pointed up the difficulty of achieving a balance between an anti-stroke regimen, which essentially involves the use of anti-coagulation drugs, and the risk of internal bleeding if the blood is too thin. All prosthetic cardiovascular devices currently in use have shown a tendency to induce thrombus formation, which not only can lead to strokes (if the thrombi break off and travel to the brain) but can also compromise the function of the device itself. Blood-thinning regimens for artificial heart recipients are complicated by the following considerations:

--The surface areas of the inert biomaterials exposed to the circulating blood is large, causing some platelet activation and accumulation which can lead to thrombus formation

--Blood flow is interrupted and very complex

--Hemolysis (red blood cell destruction), though vastly reduced since the introduction of the new UTAHDRIVE, still exists

--Infection associated with the artificial heart's implantation and routine functioning is a risk and causes changes in the blood's general tendency to clot

--A recently operated patient has a greater tendency to bleed.

Our studies have indicated that in assessing the thrombogenic potential of a prosthetic device like the artificial heart, several factors come into play, including activation of both the intrinsic and extrinsic pathways of the coagulation cascade; activation of the platelet system; activation of the fibrinolytic system; and the nature of the antithrombotic/antiplatelet regimen used. These factors interact with one another as well as with other enzyme and cellular systems in the body. The main consequence of these complexities is that, although we have improved preoperative and postoperative testing for platelet and thrombus formations, there is as yet no foolproof antithrombotic/antiplatelet regimen for an artificial heart recipient. This is a door that is already ajar; our experience suggests a detailed regimen for artificial heart recipients preoperatively, intraoperatively and postoperatively. It includes the various antithrombotic and antiplatelet medications, in addition to a laboratory monitoring schedule appropriate to each period. We believe future implants will open the door wide enough for us to eliminate strokes as a probable consequence of artificial heart surgery. Dr. Richard Ward, a scientific consultant to the program, has developed a means of individualizing dosages of heparin (a blood-thinning agent) for patients on routine hemodialysis; his technique holds promise for artificial heart recipients, and we look forward to testing it.

3. HEMODYNAMICS

The dramatic decline in hemolysis as a consequence of the "soft" pumping action of the new UTAHDRIVE system has already been related. In other areas of hemodynamics the results we have obtained have been equally exciting. It turns out, for instance, that we have been able to maintain a constant heart rate when a patient is exercising because the body adjusts to the increased circulatory demands. In other words, we have found to our surprise that the body is able to autoregulate the stroke volume of an artificial heart. When a heart recipient exercises, his heart pumps at the same rate as it does when he's at rest, but his body increases the amount of blood per beat to compensate for his exertion. So what we thought would be a problem -- the fact that our artificial heart beats at a constant rate, unless it is mechanically adjusted -- has been solved by the body's own adjustment mechanism.

Our studies of the effect on artificial heart recipients of drugs that are commonly used for patients with various heart conditions have yielded results with application to the entire field of cardiology. Dopamine is a representative example. This drug is used to heighten blood pressure, cardiac output and systemic vascular resistance in patients who have suffered heart attacks or who are being weaned from a heart-lung machine. But in patients with an artificial heart it has the opposite effect. Both Mr. Schroeder and Mr. Haydon experienced a reduction in pressure, output and resistance when given dopamine. These studies suggest several possibilities about the dynamic nature of the heart. and we hope subsequent implants will enable us to probe further its interactive role with blood circulation.

4. IMMUNOSUPPRESSION

Preliminary observations of the three JARVIK-7 artificial heart recipients at Humana Heart Institute International point to another phenomenon that is only partially understood -- the tendency of recipients to suffer severe immunosuppression in the first few days after an implant. This renders their bodies ripe for disease at a time when they are already weakened by the trauma of implantation. Experience with membranes for hemodialysis and with oxygenation systems for cardiopulmonary bypass indicate that synthetic materials interacting with the body tend to hamper its defense mechanisms. In our studies so far we have been unable to determine whether the artificial heart itself induced an alteration in the body's immune system, or whether it was due to the patients' concurrent infections, their underlying disease processes, their nutritional status or the artificial heart's interaction with their blood. We have developed a new series of tests for future implant patients in order to clarify our understanding of the artificial heart's effect on the immune system, to identify the exact causes of immunosuppression and to eliminate or control the phenomenon.

Current Status of Artificial Heart Recipients

Mr. Schroeder continues to recover from a stroke suffered Nov. 10 which necessitated his return to Humana Hospital - Audubon. He is undergoing physical therapy, occupational therapy and speech therapy. Although he is not as active as he was before the stroke, he is able to move all extremities, to recognize family members, friends and hospital staff and to speak a few words at a time. The other day his family brought in one of his grandchildren, who was born last spring. He held the baby and smiled at the baby. I have seen him like this after his two previous strokes and both times he made remarkable progress. Both times he eventually left the hospital and lived in his Louisville apartment -- the first time for a month and the second time for three months. I think he will be able to do so again.

Mr. Haydon has no neurological damage and has experienced no neurological events since a mild stroke June 9, but he remains in the hospital because of his dependence on a respirator. He is gradually being weaned from the respirator and is still very weak. The dependence arises from two factors: a mild case of obstructive pulmonary disease before surgery, and internal bleeding postoperatively. To stop the bleeding we had first to use multiple tubes and needles to drain his chest cavity, and in the course of this treatment he developed a chest infection that originated in his lungs. We are very encouraged by Mr. Haydon's postoperative neurological course. If Mr. Schroeder had been the only recipient at the Institute we might have been tempted to conclude that debilitating strokes are a necessary consequence of the heart, but you only have to go down the hall to Mr. Haydon's room to see that this is not the case. Last week Mr. Haydon went for a van ride and was taken across the street, where he spent several hours with his wife in her apartment.

In such a discussion more general questions about quality of life naturally arise. Do Bill Schroeder and Murray Haydon have the quality of life they want, or we want for them? No. Is their quality of life adequate, considering their preoperative state? Yes. As a physician I would not implant an artificial heart if I did not think it would give an improved quality of life, and it has. Bill and Murray would be dead if they did not have artificial hearts. Neither has asked me to turn off the UTAHDRIVE and end his life. Nor has Juanita Haydon or Margaret Schroeder asked for this, although I have discussed the possiblity at length with each of them and will continue to discuss it.

Last June the wives of all the artificial heart patients I've operated on -- Una Loy Clark, Margaret Schroeder, Juanita Haydon and Jinx Burcham -- were interviewed together. By that time Barney Clark was dead, Bill Schroeder had suffered two strokes, Murray Haydon one and Jack Burcham had died after 10 days on the heart. All four said they did not regret their husbands' operations and would go through them again. In December Una Loy Clark said, "I thank God for men of vision with the courage to face possible failure, but with the stamina and determination to ultimately succeed. And that's what I think we are faced with at this point" (3). In an interview published about the same time Margaret Schroeder commented, "Maybe the doctors can help with the problems the heart has caused, like the strokes. I hope the doctors can find out if the artificial heart can really work or if it is only going to be a bridge, because in the future maybe our grandchildren or their children might need it. . . I want that heart for all of us. Even for mine when it runs out" (4).

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(3) "The McNeil-Lehrer Report," Dec. 20, 1985.

(4) People, Dec. 16, 1985.

In the public concern over the setbacks and disappointments suffered by the heart patients, we tend to forget that without the heart they wouldn't be here. But they haven't forgotten. I remember the Christmas morning when I got up with my six kids and moped around the house and got all the presents opened and finally, about 10:30, my wife said, "O.K., we can go to the hospital." We went to the hospital and down to Bill's room and there was Bill with his grandchildren. He pulled us over and grabbed our hands and said, "Thank you for giving me this day." I'll never forget that. It was something that really bolstered my spirits. It's what, finally, this project is all about.

While we all want Bill Schroeder and Murray Haydon to live normal lives, we must also bear in mind that the project is about scientific research. Good scientific research is not based on one, two, four, or even a dozen cases. A researcher has to have enough of a patient base to make a wise and prudent decision about whether an experimental procedure is worthwhile. The precise number of patients needed, and the amount of time it takes to reach a conclusion, should be left to the investigator. He should be trusted to make this determination. I would be delighted if Bill Schroeder and Murray Haydon were both 100 percent healthy now, but I would not feel any differently about the artificial heart. It is still an experimental device, in the earliest stages of clinical investigation. There have not been enough recipients to make a good decision on its merit. I'm encouraged to see so many institutions engaging in clinical research, but if you add up all the clinical trials you still can count them on your fingers and toes.

And yet, the tremendous public exposure this experiment has received has created a hunger for quick positive results. No other experiment in the history of science has been scrutinized as closely by the media and regulatory agencies as this one has. Such close attention has led to a "case mentality" -- a tendency to judge the experiment in terms of how the most recent artificial heart recipient is doing. The new FDA reporting rules state this explicitly: I will be given or refused permission to do another implant based on the FDA's assessment of the previous one. I submit that this case mentality, though understandable and well-intentioned, is a threat to the scientific integrity of this or any other research project. Imagine how the history of science would have been altered if researchers, in the early stages of an investigation, had to justify its continuance by an unbroken string of successes -- as defined by others. Julius Comroe sheds some light on this prospect in the following passage from his book Retrospectroscope: Insights Into Medical Discovery.

> Trendelenberg, the famous German surgeon, wrote in 1912: "Twelve times we have done it [pulmonary embolectomy in man] at the clinic, my assistants oftener than myself, and not once with success. And yet, I would continue trying." He did and continued to be respected. Cutler and Beck remained respected physicians after six consecutive patients with mitral stenosis died postoperatively; Streider did not suffer disgrace when his patient died after his pioneer attempt to close

> her patent ductus arteriosus. Clarence Dennis was the first to try open heart surgery in man using a pump-oxygenator, about a year before Gibbon; his patient died. John Gibbon, the great pioneer in surgical research who almost single-handedly developed the heart-lung apparatus, was the first to use it successfully, for the repair of a large interatrial septal defect in an 18-year-old girl. But his first report told of operations in four patients, three of whom died. Harken and his associates were the first to replace a diseased aortic valve with an artificial valve, but of the first five patients, only No. 2 survived.(5)

Had any of these experiments been subject to a case-by-case review, they might well have been stopped. The medical advances they produced could have been delayed for many years or might never have occurred at all. The spinoff discoveries, which frequently came about as direct results of "failures," would have been permanently lost to science and to mankind. Ernest Starling, the great cardiac physiologist, has eloquently expressed the essence of scientific research: "Every discovery, however important and apparently epoch-making, is but a natural and inevitable outcome of a vast mass of work, involving many failures, by a host of different observers."

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(5) Comroe, Julius H., Jr., Retrospectroscope: Insights into Medical Discovery. Menlo Park, Cal.: Von Gehr Press, 1977, p. 134.

The FDA's mandated requirements for a bonafide research project under its domain are three. The project must have scientific merit; any device employed must be as safe and effective as possible; and patients must be aware of the risks they undergo through the voluntary informed consent process. The clinical investigation protocol and the JARVIK-7 device continue to satisfy these requirements. Since the beginning, my investigation has been characterized by the strictest compliance with FDA directives. I expect this to continue. But in light of the new case-reporting requirements it is worth noting the price of this compliance, and worth asking whether it is aiding the welfare of heart recipients and fostering scientific progress.

Over the past two months, in preparing for an FDA review of the project last December and then revising the protocol, I averaged 15 hours a day writing along with taking care of Bill Schroeder and Murray Haydon. I have committed my life to developing the artificial heart, yet I find myself wondering whether to counsel young medical researchers to enter this field. The constant filing of too-frequent reports on patient status is not what excites young people about science. Science is sparked by the challenge of creativity, and that spark can be doused by overzealous review just as easily as it is kindled by curiosity. I fear our country's leadership in medical research is threatened by overregulation. If other projects are as closely monitored as the artificial heart at Humana Hospital - Audubon, I am surprised any science is being done here at all.

In closing, allow me to pose several questions. The public demand for information on the status of artificial heart recipients has its place, but who is truly in a position to judge whether the research is effective? Scientists make this judgment. They have access to data that the public cannot get -- at least not immediately -- because it relates to patient privacy and other proprietary issues. Regulatory bodies would be well advised to evaluate a project based on scientific reporting, released when an investigator feels it is ready, and not on reports in the media. Scientists historically have had sovereignty over when to publish the results of their own research. Some have done so after one case; some have waited to complete a long series. I see no compelling reason why this should not be so with the artificial heart.

Who actually speaks for the public in its concern about experimentation? Is it the press? Bioethicists? Once again, the scientific community bears the ultimate responsibility for medical advances, because it is uniquely competent to conduct experiments as well as comment on them.

Finally, what is the real nature of the artificial heart program? It is clinical research, but it is also a microcosm of life, involving a number of important domains. It touches on legal issues of patient consent, the right to life, the right to die. It touches on family responsibilities for people who are very ill. It touches on psychiatric issues. It is an experiment with as many "soft" data points as "hard" ones. To say the only thing we are learning in this project is whether the artificial heart will work or not is to undervalue its utility, and to minimize its benefits to society as a whole.

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BIOGRAPHY

WILLIAM C. DEVRIES, M.D.

William C. DeVries, M.D., 42, is Principal Investigator for the artificial heart program at Humana Heart Institute International.

In August, 1984, Dr. DeVries joined the cardiovascular surgical practice of Dr. Allan M. Lansing in Louisville, Kentucky. He is an attending surgeon at the Heart Institute, located at Humana Hospital - Audubon, where he conducts the clinical research program on the artificial heart in addition to his cardiovascular and thoracic surgical practice.

Before moving to Louisville, Dr. DeVries was Chairman of the Division of Cardiovascular and Thoracic Surgery and a Research Associate in the Division of Artificial Organs, Department of Surgery, at the University of Utah School of Medicine in Salt Lake City, Utah. He also served as Chief of Cardiothoracic Surgery at the Veterans Administration Medical Center in Salt Lake City.

Dr. DeVries graduated from the University of Utah in 1966. He earned a doctorate in medicine from the University of Utah School of Medicine in 1970 and completed his internship and residency at Duke University Medical Center in Durham, North Carolina.

A recipient of numerous research awards, Dr. DeVries has written over 45 articles, abstracts and book chapters for medical and scientific publications and given more than 40 national and international presentations.

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Mr. Volkmer. Thank you very much, Dr. DeVries.

At this time we will recess until 12:50. At that time we will reconvene.

[Whereupon, the committee recessed, to reconvene at 12:50 the same day.]

Mr. Volkmer. The subcommittee again convenes.

At this time I would like to ask all the previous panel to the table. At this time I would like to have a few questions.

Dr. Annas, it appears from your testimony that you feel that the informed consent process that has been used in the past for artificial heart recipients is not adequate. Is that correct?

Dr. Annas. I think that's a fair statement, yes.

Mr. Volkmer. And you have elaborated it in your statement, your reasoning therefor. Are there any additional factors that would make it more acceptable that you can think of?

Dr. Annas. First, just to call the committee's attention to a piece of information I hadn't had previously which is in today's USA Today. And it's too bad Dr. Copeland's not here to tell us whether it's true or not. But he is quoted at page 3 of that newspaper as saying, about his most recent implant patient, quote: "She didn't want it. We didn't want to do it, but the alternative was pretty grim. It would have amounted to throwing in the towel."

If that quotation is accurate, that means he went ahead and did his last implant without informed consent at all, and even over the objections of the patient, which——

Mr. Volkmer. Well——

Dr. Annas [continuing]. Clearly—I mean, he's not here to defend himself, so I——

Mr. Volkmer. No. And in defense, I would like to say that, having read newspaper accounts——

Dr. Annas. I agree.

Mr. Volkmer [continuing]. Of statements that I have made, they sometimes—in other words, it could have been that she didn't want to do it and he didn't want to do it, but they'd rather have a human heart for a transplant——

Dr. Annas. I understand.

Mr. Volkmer [continuing]. But none was available. And then she fully consented, knowing everything, even though she really didn't want to do it. So——

Dr. Annas. Taken as a hypothetical, at least, I would argue, certainly that's not—I think we all agree, that's not the proper way to proceed.

Mr. Volkmer. Right. And it appears, of course, one of the main concerns is the full consent as to what can occur in the future, what happens when a person becomes incompetent or comatose, knows the chances of probably regaining their full facilities, all of these things.

Dr. Annas. I think that's very important. I think I should underline that, because that's likely to happen, predictably likely to happen.

Mr. Volkmer. And as we've heard from Mr. Schroeder—Mr. Schroeder, is it true that, as I understand your statement, that because of the nature of the artificial heart transplant experimental surgery and the complications that arise and as you've been through it, that it's not only on the patient but also affects the whole family?

Mr. **Schroeder**. Yes, I think the family is very much involved in it. I think that a person that wants to continue living, you know, has to have a reason for wanting to do that. And probably one of the big reasons is because of their family. And we were very supportive of that and we still are. We are an integral part of that, I believe, not because we have to be but because we want to be.

You know, I think that I can honestly say that not everybody is suited to have an artificial heart, that they need a strong family to help them out and that the family needed to become aware of all the situations as well as the patient on what may occur.

Mr. **Volkmer**. Yes, you said to be better prepared for the things that could possibly ocurr, in your statement.

Mr. **Schroeder**. Right. I think today, since the number of them has increased, that more and more people have become, including the doctors, have become more and more aware of what the possibilities will be. And these possibilities need to be passed along to the patients.

But, you know, there's a problem in there in the fact that, when you have someone who's going to be receiving this device, they're coming to you because they have no other alternative. Sometimes, even though you're sitting there and you're telling them the complications that may arise, they're holding on to the hope that these complications will not arise and that they will, you know, become better. So, you have to, I believe, just, you know, emphasize to them as much as you can the problems. And really the only way that I can see that you can really educate the people is through the media telling everybody basically all the different people that have gone through it. And the more that you learn from the other people, the more the people down the road are going to, you know, be better because of it.

Mr. **Volkmer**. Who participated in your family other than your father, of course, in giving the consent, in other words, in his decision?

Mr. **Schroeder**. I believe my father and my mother signed the document.

Mr. **Volkmer**. And they're the only ones that actually were present when the—on discussions as to giving the consent and the occurrence of what could occur and all that type of thing——

Mr. **Schroeder**. I believe that's so.

Mr. **Volkmer** [continuing]. Conditions.

Is that my understanding now, that after going through the process you feel that the rest of the family, if possible, should be brought in at that time, or at least alerted so they could participate in it?

Mr. **Schroeder**. You know, I think, if you're going to become involved in the situation, if you want to become involved in the situation, that you should learn as much, you know, before everything happens. Our situation was unique in the fact that the time period was short. We had a lot of media attention. And a lot of things were happening real quickly. I kind of blame myself because I didn't pursue questions that I should have asked. But a lot of times, you're more concerned about the situation at hand than you are at, you know, what might happen later.

We pretty well left the decision up to Dad. I would have liked to have been involved in the consentment form, but somebody else may not have. But the decision wouldn't have changed, I am sure, if I had been involved. The only thing would have been that I would have been more informed. I probably would have been able to handle the situation a little bit better.

Mr. **Volkmer**. In commenting on that, in the event that—in other words, that you had been informed beforehand of everything that was going on, before your father actually gave consent, it would still be the decision would be made by your father, would it not, and not by——

Mr. **Schroeder**. Definitely, the decision, it was his decision. We just supported whatever decision that he made. The information was given to him. He had to make his mind up as to what he wanted to do. We each, you know, said we supported him and told him that, if that's really what he wanted, after hearing everything that was presented to him, we would support him.

Mr. **Volkmer**. Dr. DeVries, you've heard these discussions. Sometime in the near future I am sure that you will probably be conducting another implant with the Jarvik instrument, one of them. So, since the Schroeder and the Haydon implants, have you changed your consent form, or do you plan to make any changes relative to the things like have been discussed here today?

Dr. **DeVries**. Mr. Chairman, we have seen that the consent form is not really a consent form but is a consent process.

Mr. **Volkmer**. Right.

Dr. **DeVries**. In the case of Barney Clark, literally hundreds of hours were spent talking with both he and his wife and his family about the consent. Now, Barney Clark was interesting because he said he did not want his wife involved in the process because he didn't think it was going to work. And he did not want her being responsible for something that he did to himself.

In the case of Mr. Schroeder, it was exactly the opposite. Mr. Schroeder wanted his wife Margaret, involved because he recognized the fact that she was going to be involved in it one way or another, whether she wanted to or not.

We had learned over the experiences of Barney Clark some of the complications and some of the obstacles that they would meet and incorporated that in changing the consent form from Mr. Clark's case to Mr. Schroeder's case.

We also learned that the family was important, as Mel has stated. Mr. Schroeder was specifically chosen because of the strength of not only him but his wife and his family support system. In the time between Dr. Clark's death and Mr. Schroeder, I had actually turned down patients because they did not have as good a support system as the Schroeders had. So, we actually looked at the first patient with the idea that the patient had to have a good support system. We had learned that that was important.

Now, with the experience of Bill Schroeder—and again, that took hundreds of hours of talking to Margaret and himself. It started out in a dialog, I remember very clearly, on October 25, when we sat with Bill Schroeder, Margaret Schroeder, his two physicians from Jasper, and a tape recorder. He wanted to record it so he could get information back to his kids. We discussed it at length.

After that point, daily visits by myself, psychiatrists, social workers, nurses, multiple doctors, and we basically told them just about everything that we knew about what was going on. Now, we didn't perceive that strokes were going to be as big a problem as they were. And that's something we learned. When Mr. Haydon came along, we emphasized a little more about stroke.

Along with the process of consent form, as things have happened, and we learned more of the relevance, we felt that we obligated ourselves to the family and the spouse to explain things to the best of our knowledge. And we have changed the consent form for the next group of patients.

That in itself is a difficult process, because it involves not only myself, a physician, writing the consent form; but it involves lawyers involved in it and the hospital administration. Then it goes to the FDA. Then it goes—or the IRB. Then it goes back to the FDA, and it's modifications up and down the line. A modification of the consent form can take literally months.

We felt obligated to do it. And we think that our consent form is not in its final stage and will be changed hundreds of times before it's available, and are willing to do that if necessary, because we feel that informed consent is paramount to the entire issue of human experimentation.

Mr. VOLKMER. And in the present form you contemplate using in the next surgery, do you take into account a patient becoming incompetent, unable to communicate, comatose, or a position in that regard, as to who should make decisions as to that time? Or do you take—there's other areas, too, in other words, you can anticipate and have the patient himself in the consent form make that decision. In other words, if I do, this is what I want you to do. Or you can say, if this happens, then I want this person to make the decision, or I want you to make the decisions. Those things can be done. Do you cover that area in your consent form?

Dr. DEVRIES. Mr. Chairman, we have to deal with several issues on that aspect. We deal with what is legal in the Commonwealth of Kentucky——

Mr. VOLKMER. Correct.

Dr. DEVRIES [continuing]. Plus what is legal in an institution, the IRB and the FDA. The consent form that was submitted in my record was one that actually Bill Schroeder and Murray Haydon signed. That was an example of that. We have a new one that will be sent to the FDA within the next few days that will have it a little different.

We have a little bit of problem in the Commonwealth of Kentucky, where there is no living will, no death statutes. To legally say that we can authorize a wife or a spouse to authorize treatment, to make consent for someone under that condition. What we basically do on this is that we make it very clear with the spouse and the next involved in the process that we will tend to be very sensitive to their wishes and to their desires and will be responsive to that. We feel very strongly about that.

We have not committed it to a legal statement saying that so and so will be able to effect my decisions, because, again, that is not legal in the Commonwealth of Kentucky as it stands right now. I think it ought to be. And we are working on legislation at this time.

Mr. VOLKMER. So, you are basically constrained, of course, by the legality of whatever you do.

Dr. DEVRIES. Mr. Chairman, we are constrained morally and ethically and legally. As a physician, I am caught in issues of all of those concerns. What I want basically is that the patient is informed the best he can be informed and the family is involved appropriately and that they have all the information they need. That is a hard thing to do.

Mr. VOLKMER. What about in the consent form? Dr. Wolfe, in the previous panel, had referred to a publicity clause the Humana Corp., has in the consent form. Let's assume that a patient says, I don't want to go along with this. What would be the reaction?

Dr. DEVRIES. If the patient—I think that clause basically existed because of the experience we had with Barney Clark. When the implantation occurred, we had no idea of the public interest that would be involved. We had no idea that his house would be broken into the night of surgery and his photo album taken and sold on the black market, and so forth and so on. And we were utterly astounded by the fact that suddenly a patient who may not want to be in the limelight was, in fact, himself in the limelight.

The statement in the consent form was mainly stated to say that this is the way it probably will be, to the best of our knowledge. Again, I turned down patients because they did not want their name released and they did not want to be a public figure, because I knew that they would, whether they liked it or not.

We were able to change our stance a little bit with Murray Haydon. Bill Schroeder really enjoyed talking to press and was excited about the fact of being alive. He did well on television, enjoyed it. He really thought that was a fun thing for him. But Murray Haydon was a very private person. He was afraid of cameras and didn't like to talk and things. And he said: if I'm going to have cameras thrown in my face every time I make a statement, I don't want to do it. We protected his wishes. And I must admit, the press has been very respectful of those wishes of his and stayed away from him.

Mr. VOLKMER. Dr. Annas, you mentioned in your statement having a national IRB, institutional review board, because local IRB's may not be capable of monitoring the artificial heart protocols, patient selection, may not be capable of designing adequate consent forms, processes. As I understand, you advocate the use of a nonphysician, nonscientist on this national board. Now, could you elaborate as to who you would have, the type of people you would have on this board, so that I can understand? I have a difficulty in understanding if the physicians—and I can understand how some physicians and administrators, et cetera, on local IRB's are not able to do it, because they don't have the expertise. I won't argue that. But how do you get laymen who aren't involved in a field at all to have the expertise?

Dr. ANNAS. Well, I don't think the proposal is to have people who aren't involved in the field at all necessarily involved. We have a few models, even though most of them were tilted toward scientists in some of the committees set up by Congress, actually: the National Commission for Experimentation and Human Research set up in 1974; the President's Commission, which was set up by Congress later in 1980. Both of those drew a wide variety of experts in ethics, philosophy, law, sociology, science, medicine. And the notion is not that these people be people who don't know anything, in other words, someone who has no experience in the area at all, but people who don't have any personal stake in whether or not one heart or another heart is implanted and where it's implanted, and people also who have a broader expertise than just a scientific. We have to have a scientific expertise, but these are more—most of these questions actually turn out not to be scientific; they turn out to be societal, ethical, legal, and moral questions that require really a very careful review, I think.

Mr. VOLKMER. Thank you very much, Dr. Annas.

I now recognize the gentleman from California for questions.

Mr. PACKARD. Thank you, Mr. Chairman.

Let me follow up with the question just asked, because it was certainly one that I had. I could not help but see the flashing lights come out of your testimony, your written testimony, when it spoke of nonscientists and nonphysicians. I can't believe you mean that, frankly, and apparently you don't——

Dr. ANNAS. A majority, a majority, not——

Mr. PACKARD. And apparently you don't, from what you've just said, that they do have to be scientifically oriented, but——

Dr. ANNAS. It depends how you define scientific——

Mr. PACKARD. But what I perceive from your testimony—and that was a portion of it—is a recommendation to remove this whole decision-making process as to how far—and whether we do it at all—we move in this experimental process of heart replacement or heart assistance, and transfer that responsibility to society. And that gives me great concern. I don't really look upon society as being the place for us to make these decisions. It is a transfer, in my judgment, of personal rights and personal welfare to government, to society; and I am not an advocate of that by any stretch of the imagination.

But be that as it may, it certainly does bring up some important questions, I think.

Dr. ANNAS. May I comment on that briefly?

Mr. PACKARD. Certainly.

Dr. ANNAS. I don't think it's a new transfer. Technically, the current law requires the local IRB to do just that. And all that this proposal would be is to recognize that the local IRB can't do that, and that what they can't do, is important to do. And so, we should give it to someone who can do it.

Mr. PACKARD. If society is to have the control and the authorization responsibility of all decision making in these kinds of research programs, I think the question has to be asked, and you've recommended that we halt, we halt the experimental process and the implantation until we have significant answers to, I believe—oh, let me read to you what I saw in your testimony: Because the rights and welfare of potential subjects of experimental artificial heart implantations are not being adequately protected, I strongly believe that there should be a moratorium on all implants until their scientific reasonableness, proper use, clear patient selection criteria, adequate informed consent procedures, clear rules on stopping individual experiments have been developed and approved by joint review—et cetera. And all that should be stopped until these are all answered.

I guess the question has to come, at what point would you then authorize or recommend an authorization of moving forward with the experiment?

Dr. **Annas.** When this committee was satisfied that it had a reasonable, scientific basis to go ahead on humans, when the consent procedures were reasonably in place, and when the patient selection criteria procedures are reasonably in place.

Remember, every witness who has testified about going ahead has assumed, their assumption has been, that we are currently getting adequate informed consent, that our current patient selection criteria is adequate, and that it is scientifically reasonable to go ahead. I disagree with those things, but it seems to me that what we need is not me saying that or them saying that, but a representative cross-section of people appointed by NIH and FDA who are ultimately——

Mr. **Packard.** But has not the——

Dr. **Annas** [continuing]. Funding and regulating this to do that.

Mr. **Volkmer.** If the gentleman will yield just on that point.

Mr. **Packard.** I would be happy to yield.

Mr. **Volkmer.** I think you just mentioned the last part. We presently do have an organizational structure in place that does review all this and does have to give its approval. And that's the NIH and FDA.

Then what really comes through, Dr. Annas, that you basically disagree with those two organizations, that these things are in place as they should be. Is that correct?

Dr. **Annas.** You have two things on that. First of all, it's not clear to me—I mean, they're going to testify for themselves whether they really think that the current situation, at least regarding temporary artificial hearts, is adequate. I will let them talk to that. But the second thing is, both of the agencies actually have different missions and see themselves as having different missions. FDA is a regulatory agency. NIH promotes research. And they do have different missions. On the other hand, I believe they are both so involved in this particular experiment of artificial hearts that there really needs to be not just informal communication between the two agencies but formal communication on this level. And that's really what I am recommending. Not that we change the law in the sense of what the rules are, but that we set up a reasonable way that these agencies can implement the law together.

Mr. **Volkmer.** Well, what I get, though, from the discussion that you had in your statement about this committee, you really want—you didn't say do away with the NIH and what they're doing——

Dr. **Annas.** Absolutely not.

Mr. **Volkmer** [continuing]. Not change what FDA's doing, but we're going to have also now another committee out here that is going to be basically setting up the IRB.

Dr. **Annas.** Going to be replacing the local IRB for these particular highly controversial——

Mr. **Volkmer.** Experimental——

Dr. **Annas.** Exactly, that's exactly right. You got it.

Mr. **Volkmer.** OK. Now, would that also be subject to review by the FDA, as the local IRB is?

Dr. **Annas.** Could be——

Mr. **Volkmer.** Or would it be——

Dr. **Annas.** It would be a creature of the FDA and the NIH. So, in that sense, sure. I mean, it would theoretically—I guess theoretically it would be an advisory committee to NIH and FDA and the local IRB's.

Mr. **Volkmer.** That's a little bit different than what you originally said in your statement. As I understand, you are going to replace the local IRB which basically formulates and then sends it to FDA for approval.

Dr. **Annas.** I guess I wouldn't say replace so much as supplement. You'd have to go through the joint committee. I really don't care whether you, after that, required local IRB approval or not, because I don't believe local IRB approval means much one way or the other. I would be perfectly happy to continue to require that, perfectly happy to do away with it. What I think we need is a review committee that can really do the review that's needed in cases like this.

Mr. **Volkmer.** Well, my question still is, would they replace the function that FDA presently does, or would it just, say, supplement it, have another stage to go through before it——

Dr. **Annas.** I guess, you know, before that question is the question, what function that FDA currently does do you think it might be replacing? Because the FDA tells the public and tells me that they rely on the local IRB for issues of consent and patient selection. They are not making those decisions now. And this would force them to become more involved in those decisions.

Mr. **Volkmer.** OK. All right.

I yield to the gentleman from California.

Mr. **Packard.** Thank you.

To your knowledge, Dr. Annas, have other human experimental processes that now have become rather commonplace, kidney transplants, multitudes of other transplants, for that matter, pacemakers, coronary bypasses, and a lot of the lifesaving mechanisms that we now use, would they be now in function and become a way of life for our medical health care providers, had they been required to go through the same requirements that you're recommending that this experiment go through? Or would we still be waiting for those to emerge from the experiments?

Dr. **Annas.** It is absolutely possible that we could slow down the introduction of some medical devices and some procedures into the health care system. But I don't—if the purpose of this is to protect human rights in the meantime, I think that's a small price to pay.

Mr. **Packard.** My own background has led me to do some experimenting with the human body. I have learned that much of what you need to do in terms of regulation, in terms of control, in terms of reevaluating your procedural methods, comes out of the very process of experimenting. Often you don't even know what needs to be done until you are into the experiment and have some responses and reaction, and you haven't time to evaluate what you've been doing in terms of the very things you brought up. So often, isn't there going to always be in the experimental process the need to go back and evaluate what your experiment is unfolding and revealing to you in terms of regulation, in terms of procedures? And therefore is not the experiment necessary to move forward and complete it before you really know what you need to do in terms of the things you're concerned about?

Dr. **ANNAS**. Some are and some aren't. As I said, the original implant in Dr. Barney Clark is arguably justifiable because you had no way to know how it was going to come out, all right. Dr. DeVries just said previously that he thought Dr. Clark would either die relatively quickly or go home in a relatively short period of time and lead a——

Mr. **PACKARD**. I think that's true with every patient that has had that dealt with.

Dr. **ANNAS**. But that turned out not to be true, and I am sure he wouldn't say that again to another heart implant patient, because we know that there is almost no probability of that. I almost said no, but there's always some probability of anything. So that, as you learn that, you're absolutely right; you should change things. I think the consent process, the consent form should change. I also think at some point we may learn enough to say: Hey, we shouldn't do that anymore. And there's no mechanism really in place to say that now.

Mr. **PACKARD**. I think, if I understand the testimony that we've heard thus far, however, of those that are involved in the program, it is clear that they are reevaluating their consent forms. They are evaluating their mechanical devices. And they are evaluating their successes and their failures.

Dr. **ANNAS**. I think——

Mr. **PACKARD**. That really is experimentation at its best.

I guess all I am trying to say is that the worst decision in experimentation, in my judgment, is to stop the experiment when you see failure or when you see problems. And that is not experimentation. And to stop it in the middle of an experiment before you come to conclusions, before you determine what the problems are, and what the failures are, and the successes are, often will lead you to no conclusion and no results if you stop in the middle of an experiment.

So, that's why I guess I have some problems with your testimony and your recommendations. But let me get to Dr. DeVries.

In your procedures thus far, have you been able to determine an average cost for the implantation of your Jarvik-7 device?

Dr. **DEVRIES**. In the case of Barney Clark, his hospitalization totaled approximately $250,000. That was at the University of Utah. We have not figured that cost out at Humana yet. We simply have not got enough patients, I think, to determine what the average cost would be. We have done it in three patients. And one of the things that we are very interested in—while we are very concerned about cost containment, we look at this as a clinical experiment. As long as Mr. Schroeder and Mr. Haydon are alive, their contribution, their decision to enter into an experiment deals with the fact that we will use their time to the best of our ability to obtain scientific data.

With that, we have spent, really, many thousands of dollars, spending money in order to develop the most acute and chronic and best coagulation study and evaluation procedure so that we can see every single thing that is going on, that we don't lose any information or data. So, we have actually escalated, I would say, the costs on these patients. During the initial period of clinical investigation, it is absolutely critical that we do not spare money in order to determine what is a benefit and what is not a benefit. We need to know in these patients how to prevent strokes or other, so it will work. If we develop a device that doesn't cause strokes, that would be much more cost accountable in the future in the long term because of the money we've put into it now than it would be later in order to save things.

So, we have none—we are very aware of the fact that in the early future as soon as this device has become effective and we show that it can work and we can make it a good quality of life, that we are going to have to be very accountable for our costs. And we understand that cost containment is going to be a very strong issue.

Mr. **PACKARD**. Who bears the cost of the——

Dr. **DEVRIES**. Humana is paying for the——

Mr. **PACKARD**. The hospital?

Dr. **DEVRIES**. The Humana Corp.

We believe that the patient is involved in an experiment, and he shouldn't have to pay for that experiment on himself. We don't believe that the Government should have to pay for it right now, and there's a private corporation paying for the experiment. And I think that's the way of the future.

Mr. **PACKARD**. Mr. Schroeder, in your case, your father's case, has the process cost the family anything other than incidental issues, but as far as the medical care itself?

Mr. **SCHROEDER**. No, Humana has been real good at providing all the financial background. The only thing that we've had to, you know, pay is the trips back and forth and the meals and things of that nature.

Mr. **PACKARD**. Thank you.

Mr. **VOLKMER**. Will the gentleman yield on that?

Mr. **PACKARD**. I would be happy to yield.

Mr. **VOLKMER**. This relates to it. Involved here at the present time are funds from NIH, are there not?

Dr. **DEVRIES**. No, sir. The NIH has put millions of dollars into the clinical development of animal models. And they have been supporting the early years and years and years of the workings into a clinically acceptable Jarvik-7 ventricle. So, I would say public funds went in the development——

Mr. **VOLKMER**. At the present time, in the case of Mr. Schroeder's father, Barney Clark, Haydon and those, there's no Federal funds actually involved in paying the costs?

Dr. **DeVries**. The entire cost of the hospitalization and the experiment at Humana is paid for by Humana. There is no Federal funds involved in either of those patients' care right now at this time.

Mr. **Packard**. I understand—if the gentleman would yield back——

Mr. **Volkmer**. Yes.

Mr. **Packard**. I understand that it has been some time since Federal Government funds have been involved in the recent clinical procedures. Is that correct?

Dr. **DeVries**. In the case of Barney Clark, some of his hospitalization—I don't recall exactly how much—I can tell you was paid for by Medicare, but that was not due to the—we had to very carefully exclude any cost due to experimentation on an unapproved device or approved device. He was—I think the Federal Government did pay and Blue Cross did pay for some of his workup initially, and which was treating his underlying heart disease. But as soon as he became a patient in an experimental project, funding then left the public sector and became a matter of raising funds from private sources.

Mr. **Packard**. So, private grants and hospitals have absorbed the costs.

Dr. **DeVries**. That's exactly right, sir.

Mr. **Packard**. I'm sure one of the objectives of the procedure is assuming success will become more and more prevalent, to make it available to any patient that needs it on an equitable basis. How is that going to be done? Right now, it appears that, because of the expense, it would be reserved only for the elite, for the well off. How is it going to—in the future as you perceive the process, is it going to become available to the average citizen?

Dr. **DeVries**. Congressman, first of all, I think——

Mr. **Packard**. Without Federal funds or without public funds.

Dr. **DeVries**. Yes, sir. I think that, first of all, we have to answer to scientists. I have to answer the question, will it work, what are the complications, what are the benefits of that particular device? If for a fact it doesn't work and it's too complicated, then the public will not want it and does not need it; and it will be abolished. So, assuming that it is successful and we do show that it works and we can show that it is cost containable, then we have to say, what are the costs of it? Then those issues are going to have to be addressed sooner or later by society. It will have to be paid for from Federal grants, funds, or from third-party payment.

I think those are issues that we ought to start looking at as we get out of the early and initial investigational phases and decide at that point who is going to bear the cost. It is possible that we may make a device that the public can't afford. And that is very possible. But again it is also possible that we can save hundreds of thousands of people's lives by the device. At this point, it's too early to determine which is which.

I am saying also that the trick to determine whether the device is affordable or good to society has a tremendous value in spinoff technologies that can save literally hundreds of people's lives in unrelated fields altogether because of our trip to and from the investigative wishing well.

Mr. **Packard**. Let me turn to you, Dr. DeVries. Would you indicate how much paper work is generated in the processing of this, in order to get authorization?

Dr. **DeVries**. When I started working with the artificial heart, and when I first started working with the idea of the clinical implantable artificial heart in 1980, I started writing; and I have not put the pen down till last night, after the State of the Union Address. It really has been a very enlightening situation for me to put down on paper some of the things, and create documents such as the informed consent and then go through the experience with the lawyers and back and forth, and the legislators, and the hospital administrators. It becomes sometimes, a very burdensome thing. I can remember over the past 2½ months literally taking 4 hours off Christmas morning out of the hospital and then going back most of the time, spending very few nights at home. But again, that's what's required to do. I have a tremendous commitment for Bill Schroeder and Murray Haydon and to see the project go. And if that's what it will take, that's what I will do.

Mr. **Packard**. Is it all necessary, in your judgment?

Dr. **DeVries**. I think the frequent review and going through the number of panels that I have had to review have been good for the project. But again, I look at it a little bit like a car going in for, instead of a 5,000-mile checkup a 500-mile checkup, because after a while you find out that the car's in the shop more than you can drive it to work. And that many times is the feeling of frustration I have.

Mr. **Packard**. How long does it take to process, to get an approval to proceed with an operation at the present time?

Dr. **DeVries**. Well, the——

Mr. **Packard**. How many days?

Dr. **DeVries**. The first—you mean from the very first time I see the patient, or to get the project going?

Mr. **Packard**. Well, let me ask it a different way. Is there a difference in processing a chronic patient and an emergency patient, as far as paper work is concerned?

Dr. **DeVries**. I can only address the chronic patient. All I can say is, as far as regulatory control and paper work, I have been doing it almost constantly since 1980.

In my hospital, my institution, they do not allow me—the institutional review board does not allow me to do an emergency use. So, I have not had to cross that bridge at this time. However, most of the paper work for the emergency use would be done in the meantime.

I think in a case-by-case review the first case of Barney Clark took about 2 years of review in all different levels to get approval.

Mr. **Packard**. Well, obviously a patient can die in 2 years.

Let's ask how long Mr. Schroeder—and then I would be interested in knowing how long the emergencies performed this week have taken. Now, of course, you're not involved in those, but I think—all right, Mr. Schroeder. How long did it take to process? Dr. DeVries, how long did it take to process Bill Schroeder's?

Dr. **DeVries**. We had approval to do Mr. Schroeder, and it took approximately 3½ months to get the hospital ready to participate in the experiment. We met Mr. Schroeder for the first time on October 25. We did the operation on November 25. It took about a month in order to get him into the system, process him, work him up, and inform he and his family of what we were going to do to get on with the project. But at that time all of the regulations from the IRB and the FDA had already been met and fulfilled. And what we were doing, in essence, was fulfilling the protocol requirements that we had set and determined and provided with help of the IRB and the FDA.

Mr. **Packard**. How is that going to accommodate an emergency situation which obviously we are going to have to deal with at some point in time if this procedure is to become an emergency treatment?

Dr. **DeVries**. As I understand the emergency use, I would expect that the institution be fully trained to take that step beforehand, and then approach the patient, who is literally within probably hours of death, and go through at that time an informed consent process of some sort, depending upon how involved you wish to get it, dealing with issues of whether the patient was unconscious and able to make the consent or not, or whether the family members would, and how much of an informed consent you do.

Then as I understand it, and I am not entirely clear on this, you would have to go through a group of approvals from the institutional review board as well as the FDA, as well as the manufacturer, involving those three parties. And as decisions like this usually occur at 3:30 in the morning, that would be almost prohibitive.

Mr. **Packard**. Thank you.

Let me turn to Mr. Schroeder if I may please. In hearing your testimony and also reading some of the background of your family, it has certainly changed your family life style, this whole process. What recommendations would you make or would you give to better prepare families to cope with the problems that follow the implant?

Mr. **Schroeder**. That's a pretty tough question. A lot of it we've just experienced as we went along, and every—I would say every situation is going to be a little bit different than what ours is. Hopefully, you know, it could be better. But I think you need to get either your doctor or possibly a legal type of person to come in and look over your consent form or at least point out things to you that you might not see at that particular time because you're concerned about the thing at hand, what's happening right now. You're concerned that you have a loved one that is on the verge of dying. And you're not thinking about what might happen 2 or 3 months later. You're worried about what's going to happen tomorrow.

So, I think, basically if you could get someone that is impartial and that could maybe point out some things just so that you understand them as best as you can, because there's no way that you can tell everybody everything. You've just got to tell them as much as you can.

Sometimes you need to have somebody to ask the question for you, because you can't think of the question to ask until it's too late to ask the question. So, I think basically that would be the best thing. I would recommend that you have an impartial person possibly there to help you ask some questions that you may not be able to answer, or ask.

Mr. Packard. I appreciate that.

From your perspective and that of the rest of your family, would you agree with some of the testimony today that the process ought to be put on hold until we can answer questions that may or may not be answered at the time? Would you suggest that, as a family member?

Mr. Schroeder. Well, you know, we had some rough times. There's no doubt about that. But you almost had to be at the hospital for the first 18 days before the first stroke, and you had to see how well that the whole system worked. I envisioned tremendous problems with maneuvering and things of this nature, which is difficult, but it can be done. If you have a healthy person that is capable of moving around, it is done quite well.

I think that you need to continue on with it so that you get away from things like a 350-pound Utahdrive system and to more of the portable systems to actually find out if it's going to work or not. At this point it's hard to really say whether or not it's going to work. Let's say you leave the hospital and go home. There's a lot of questions there. We've run across a lot of situations living outside of the hospital that have been answered, and there's probably a lot more that need to be questioned.

So, you know, I think if we can continue on and eliminate the strokes and see how a healthy person can live with an artificial heart, if that's possible, and then determine from that whether or not, what kind of quality of life you're talking about, and this nature. Basically, when we went into it, I was at the very first meeting, and the things that we talked about were the quantity of life and the quality of life. We talked about what basically we hoped we could achieve from it. I think in those first 18 days we achieved more than what we thought we would. Throughout the year, we achieved what we thought we would, and sometimes we didn't. So, it was a kind of a roller coaster type of effect as far as what your quality of life was. Certain days it was great. Certain days it was okay. And certain days it was poor.

Mr. Packard. I think that's true with all of us, without an artificial heart.

Thank you very much. I will yield back.

Mr. Volkmer. I have a few additional questions. Dr. DeVries, I may have misunderstood, but on the previous panel, Dr. Wolfe at least led me to a conclusion that, due to the fact that there had not been a permanent implant in approximately 10 months, that one of the reasons, or perhaps the reason therefore was that those who would qualify under the criteria set down can now all be taken care of with donated hearts, and therefore—by transplants—and therefore we'll probably not see a permanent transplant again.

Do you wish to comment on that?

Dr. DeVries. Yes, sir. I think that it's been 10 months since we have done an implant. The reason we have waited that long is we are waiting for the right patient. I don't understand, I have not—I do not have a legal moratorium placed on me, and I have not had an implied moratorium on me personally. I am waiting. As soon as I find a patient that is as good as Haydon, Schroeder or Burcham, I will do it again.

We have had some difficulty, though, in the fact that transplantation guidelines have improved. Now more than ever, we are starting to do patients that are 54, 55, and 56 years of age. When Mr. Haydon had that decision, there was no choice available at that time.

Let me reiterate, though, that at the time that Haydon, Schroeder, and Burcham and Clark made their decision for an artificial heart implantation, there was no option available. All of them had been turned down by multiple heart transplant programs. All of them had experimental drugs used on them. And there was no other option. It was a device of last resort at that time. Since that time, we have looked for a patient that is the right size. We have been concerned that Mr. Burcham died because the device probably was a little too big for his chest. We have been encouraged with some of the work of the small Jarvik ventricle. I must admit that, if that small Jarvik ventricle had been available over the past 10 months, we probably would have done another three or four.

Most of the patients that we see are under 170 pounds and are smaller than Mr. Burcham. So as a result of Mr. Burcham's, our loss by losing Mr. Burcham, we learned that size was critically important. We immediately lost a group of approximately 70 percent of the whole pool size. So, I just say from size alone and increasing transplantation, there just frankly has not been enough.

I also think that another issue why there has not been enough other artificial hearts implanted, is that the public media, by talking about the strokes, have scared people away. And I think that's an issue. That may and may not be appropriate. I am not here to say. But I can say that that issue probably has had effects in the decisions.

We had around one or two patients a day, patients applying for the heart. And then around July, in early summer, after the strokes, it's already been coming, obviously, we now have one to two a week. So, the interest has fallen off by the medical profession as well as patients. And again, that may be appropriate or may not be appropriate; it's hard to say.

Mr. **Volkmer**. Just to clarify for the record, I know it's obvious to you, but to clarify it for the record, the patients that do apply are referred by their physicians, is that not correct?

Dr. **DeVries**. That's correct, yes, Congressman.

Mr. **Volkmer**. I mean, they just don't write you a letter and say I'd like to have one of your artificial hearts?

Dr. **DeVries**. Yes, sir, we have about a third of the patients apply themselves. About two-thirds of the patients apply from a cardiologist or their doctors. Those that apply by themselves, we ask them to get ahold of their doctor and have the doctor apply. So, all patients come to us as they're referred from their physicians initially.

They're usually—we check them out as far as whether they are appropriate candidates, sizewise, diseasewise, associated diseases. The ones that look like they may be a good candidate are brought into the hospital. After evaluated by the hospital, we feel it is mandatory to reject them as transplant patients before we proceed. So, they go on to the transplantation registry. They are evaluated by the committee to determine whether or not they are a candidate. If they are not a candidate for a transplant, then we'll enter the scene again, finish up all the evaluation on them, and then have a meeting where we have the evaluation committee determines how long a life they've got, what their risks are, how good they are at fitting into the protocol.

After all of those decisions are made, we present the option to the patient. Then we start the informed consent and then go on with the project. There is a tremendous amount of controls and restraints of different kinds before the final patient is selected.

Mr. **Volkmer**. But at this time you do not have a prospective patient?

Dr. **DeVries**. I have several patients that have contacted me, and we're still looking at them. But there's not one that is——

Mr. **Volkmer**. Been approved?

Dr. **DeVries**. No; no one has been approved at this point.

Mr. **Volkmer**. Along with all this other work that you have been doing—and you sound quite busy—I would just like to ask if you also are a practicing cardiovascular surgeon in that timeframe?

Dr. **DeVries**. Yes, sir, I was until about 3 weeks before the FDA's last call, when I attended the advisory circulatory meeting. At that point my volume considerably decreased to about one case a week. I have had to do almost, well, essentially full-time work since the early part of December until this week, which amounts to a total of probably about 18 hours a day doing nothing but paper work, and about 15 minutes a day taking care of those two patients.

I have had essentially no time for a private practice at this point. I look forward to getting back because that's what I really am. I'm a heart surgeon, and I enjoy clinical care; and that's what it's all about.

Mr. **Volkmer**. Now, you agree, to look overall at the heart transplant picture instead of the implant picture, that we still have a shortage of donors for the demand at the present time?

Dr. **DeVries**. No question about that, because it is estimated by many groups that as many as 10 to 15 thousand Americans a year die of heart disease, chronic end-stage heart disease, that could be candidates for heart transplantation. If you use all of the best allocation of ability to get all the organs you can, you probably have a pool somewhere of about a 1,000 to 1,500 hundred. So, you have really about 10 times as many needed as we will be able to get.

As mandatory seatbelt and headgear regulations increase, our donor population is going down from that. So——

Mr. **Volkmer**. As long as we don't have the accidents, et cetera, and the deaths, that still preserves the heart.

Dr. **DeVries**. That's correct.

As you have the public interest by mandatory compliance to safety and automobile regulations, you're going to have decreased number of heart transplants performed.

Mr. **Volkmer**. Dr. Annas, in light of that, do you also agree that, even though the number of donors have increased in the last few years, we still have a short supply of donors for transplants?

Dr. **Annas**. There's no question about that.

Mr. **Volkmer**. All right. Now, as we implant more temporary, we saw three this week, and as we do more, those are ones that—there wasn't any readily available. If they didn't get the emergency implant, there would be a strong possibility that they would be deceased and therefore no longer need one. But now they're alive and they need one. So, we have increased the numbers, haven't we, of the donors that we need?

Dr. **Annas**. We have increased the number of donors that we need, right, without increasing the supply.

Mr. **Volkmer**. Right.

Now, but we have a permanent heart—temporary can keep them alive for a while, anyway.

Do you want to comment on that condition that we find ourself in, as to, is that a positive or a negative?

Dr. **Annas**. Well——

Mr. **Volkmer**. I guess it depends on who you are individually.

Dr. **Annas**. It certainly does.

Mr. **Volkmer**. What about society?

Dr. **Annas**. I mean, you're right. It does depend on who you are and whether you're a physician or one of the patients who needs a temporary heart or a physician of one who doesn't have a temporary heart available whose patient needs a human heart. But on a system-wide basis, there's no question that until we have some reasonable way to allocate human hearts, we're in an untenable position. Because it's unfair, it seems to me, to put the person on the artificial heart first in line just because they're on the artificial heart. Whereas, the person who would be first in line otherwise may die because he or she doesn't get the heart.

I mean, that's the reason. The reason that these things don't save any net lives is the reason why the vast majority of heart transplant surgeons in this country do not use and have publicly said that they will not use temporary artificial hearts until something can be done about the supply of organs. Dr. Norman Shumway, who is the premiere heart transplant surgeon in the country, has said that time and time again: because temporary artificial hearts don't save any net lives, they're useless to him and to his patients. They are just going to change the identity of which of his patients are going to die on the waiting list. The real public issue is how to, No. 1, increase the supply; but if you can't do that, No. 2, how to make a fair allocation of the human hearts that are available.

Mr. **Volkmer**. Dr. DeVries, would you like to comment on that? It's not necessary if you——

Dr. **DeVries**. It's interesting to me that Dr. Shumway's group, Phil Ouer has done several of these bridge-to-transplants in an effort to help his patients that die on the waiting list. At Stanford it is estimated they—well, they specifically say that one-third of their patients die while waiting, while sitting around in a motel in Palo Alto, waiting for a heart. And those are issues.

The other issue is that I agree, you may implant an artificial heart and use it for a temporary. But what if something happened, as you stated earlier, and the patient develops an infection or a mild stroke or if the patient——

Mr. **Volkmer**. Kidney failure.

Dr. **DeVries** [continuing]. Does not have—kidney failure, or even if the patient is not able to get a heart donor, such as many O-positive heart patients wait a long time. We had a man that waited 12 months at our hospital for an O-positive heart. In these patients a temporary device then becomes a permanent device, whether you like it or not. I have a real problem with offering a patient a temporary device only. And I'm fortunate that at our institution, we're able to do permanent devices, because I think it involves informed consent. If the patient signs up for a temporary device and suddenly becomes a permanent device, then he has not been properly informed. And I am just glad that the project that I have had involvement with has those things, and they do have covered permanent living quarters. And they do have covered ways to get around and the fact that the patient's needs will be taken care of. Because many times, permanent devices will be--temporary devices will become, out of necessity, permanent implantations.

Mr. VOLKMER. Now, Dr. DeVries, I have a couple more questions before I conclude. One is, it is my understanding that you have not published the results of your experiments other than the Barney Clark experiment. Is that correct?

Dr. DEVRIES. No, sir, that is not correct. We now have--it's been published by several papers. We have several peer review publications right now that are being presented.

We have presented our data probably to a group of eight or nine international symposiums and presentations within the last year. We have seen people that are working in this field from all over the world. I haven't seen Dr. Wolfe at any of these, but I have seen many that are physicians that work with me on this.

When it is appropriate to report your data, is a whole other issue that needs to be addressed, I think. There are academic surgeons and academic physicians that feel that nothing should be reported until after the full series of seven be done. But now there is a tremendous outcry from physicians that incomplete or unanalyzed data should be presented to the medical community, even though it is not conclusive and results are not out.

I think when the public outcry demands that an investigator publish premature data is a difficult situation for the scientific community to understand. And in a way, we are bending to that cry a little bit and putting in a conscientious effort to get it out as quick as we can. But we have never hesitated to share our data with any clinical investigators. I correspond freely with Dr. Copeland, Dr. Joyce, Dr. Sim, all the people, my colleagues; Dr. Pierce, who represents a competitive device; and we freely dialog among that group. And we will continue to do so.

Mr. VOLKMER. Following the seven that have been approved by the FDA, do you contemplate at that time to—of course, I am sure you will—make a full public report——

Dr. DEVRIES. No, sir.

Mr. VOLKMER [continuing]. Of the total experiments and your conclusions?

Dr. DEVRIES. Right now, the reporting mechanisms are that we report to our institutional review board on a monthly basis of all of the complications, all of the results and the scientific things that are going on there. We have reported to the FDA several times during that period of time. We are in constant communication with frequent reports to Symbion. We now have—I estimate in the next 6 months we will probably have five or six articles in the national publications that anybody can read, these are peer review articles. They have appeared now in several publications already.

I have no plans after seven patients to make a full public discourse on the experiment. I don't think that's really necessary and called for, but it will be published in multiple times.

The important thing is that we feel we have a great obligation to society and the medical profession to educate them on what we have learned. And we plan to carry out that obligation.

Mr. **Volkmer**. What effect, Dr. DeVries, will the FDA decision have the recent decision to permit you to proceed but only on a case-by-case review basis?

How do you see that affecting your research?

As I understand it, it is only partly you could do it through—once every 3 months, something like that?

Dr. **DeVries**. Yes, sir.

The formal FDA recommendation was that we submit the revisions for protocol; we did that several weeks ago.

And now we are waiting to hear from the FDA, whether they have accepted the revisions of protocol, or asking other questions, or want us to go ahead with the new revisions.

But it has been difficult, and we have had patients that we have looked long and hard at, that I would think that, you know, in the long run these regulations are appropriate, in the fact that it has helped us to get our counseling group a little tighter controlled, analyze the science a little bit.

It has slowed down the publication; I have had to address all my issues toward regulatory affairs, and none toward publication and research, in the last while.

And I think in the long run that, as my opening statement said, I think that this will slow down the scientific development, and has slowed down the scientific development of the device.

Mr. **Volkmer**. We thank you.

All right, no further questions

The gentleman from Utah have any questions?

Mr. **Monson**. Just two, Mr. Chairman.

Mr. Schroeder, do you or have any of your family members had any misgivings with the informed consent process that you went through?

Mr. **Schroeder**. I don't have any misgivings other than the fact that if—that we—as I stated in my opening remarks, that we as a family just did not sit down and look at all the possibilities, and really investigate them, and decide for ourselves what we were going to do that time.

We pretty well had to address each situation as it came up, and decide what we were going to do from there. It would have been helpful to have known beforehand if the situations would arise what we were going to do.

But, you know, basically this was a decision by my father, and I know he went through 2 weeks of intensive review and many doctors came in and saw him, and I was just not involved with it mainly because I have a family, and I have a job, and I wasn't able to be there for 2 weeks, next to his side, and go through the whole process, which they did.

Mr. **Monson**. And your father, has he expressed any misgivings about the process?

Mr. **Schroeder**. My father is a very determined person, and I have not yet seen indications from him that he is willing to quit from this experiment.

Mr. **Monson**. And, Dr. DeVries, based on information that I have seen and the statements I have heard you make, some of the effects of Government regulation have been frustrating, I think. Have you outlined in your mind, or on paper anywhere, what you think would be an adequate degree of regulation and allow you to go ahead keeping in mind the balance that, I think, Congressman Packard spoke of in his opening statement to insure the well-being of the patients, as well, and could you share that with us?

Dr. **DeVries**. Thank you Congressman Monson. Yes, I have.

I think that the Federal guidelines are adequate. I think that insuring the fact that the patient is informed, that the risk and the benefits are in adequate balance, and that there is adequate science to be learned from the experiment.

And I think that those are the calls not only from the FDA, they are also from the IRB. I think that they are appropriate.

I don't think the issues that they should be concerned about are whether there are societal costs, the effect of society in the future, any of these issues, or public opinion, should be addressed in them. And as far as I can tell they are not addressed in those bodies.

I think it is appropriate that the IRB and a local group make the decisions and go over the institutional review board very carefully, and ask the scientific questions and formulate from the institutional view with peer review at a local level and the credential of the physician and the institution, and whether the project is—or the protocol changes are effective.

At that point I think it is totally appropriate that the FDA become involved in it. They have a unique position because of their resources and their knowledge to compare multiinstitutional concerns, and they have information on heart valves that local IRB's do not have. I think it is also in their requirement to look at the different institutional review boards to determine whether or not they are appropriately working on the consent form, and whether they are duly constituted.

And I think that is appropriate.

My only concern is the interpretation of that sometimes goes over into the fact that you spend all of your time regulating, none of your time doing anything. But I do realize that this is a highly visible, and an exciting, and a sexy field, it has a lot of things that other scientific projects don't have.

And I would just ask that IRB's and the FDA evaluate in a fair and consistent manner on all projects, and according to all institutions. As long as that goes on I think that the actual working is perfectly appropriate. I do not feel that we need another regulatory body to determine consent or anything else. I think it is fully contained in the constitutional alignment of the device amendment law.

Mr. **Monson**. Thank you very much, Mr. Chairman; and I thank you for allowing me to participate, and I am going to excuse myself to attend another commitment.

Mr. VOLKMER. Thank you very much.

At this time we will excuse this panel. And I want to thank all of you for being here and you have been very helpful in our deliberations and I appreciate your testimony.

We will now proceed to the third panel.

Dr. Claude Lenfant, Director, National Heart, Lung and Blood Institute, NIH; Dr. Charles McIntosh, National Heart, Lung and Blood Institute, NIH: and also Mr. John Norris, Deputy Commissioner, Food and Drug Administration.

Gentlemen, I would first like to mention that your statement that you furnished to the committee will be made a part of the record, in full, as you appear, and you may either summarize or review your statement in full, or however you so desire.

We will begin with Dr. Lenfant, and then Dr. McIntosh, and then complete with Mr. Norris.

Just a moment, does somebody have a time constraint?

Well, let's see, Dr. McIntosh, Dr. Lenfant, you have any time constraints. I know you would like to get out of here as soon as possible. Everybody would like to do that.

But other than that do you have to be somewhere besides back at the office?

Would you be agreeable with us proceeding with Mr. Norris at this time?

VOICE. Oh, certainly.

Mr. VOLKMER. All right then, fine, we will proceed in that method then.

STATEMENTS OF CLAUDE LENFANT, M.D., DIRECTOR, NATIONAL HEART, LUNG AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH; CHARLES L. McINTOSH, M.D., Ph.D., CHAIRMAN, CIRCULATORY SYSTEM DEVICES ADVISORY PANEL, U.S. FOOD AND DRUG ADMINISTRATION; AND JOHN A. NORRIS, J.D., M.B.A., DEPUTY COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, U.S. PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY DR. KSHITIJ MOHAN, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Dr. LENFANT. Mr. Chairman, I propose to be fairly short since my full written statement will be introduced in the record.

What I would like do is briefly describe the statement and highlight some of the points of it.

Our statement describes six issues.

First, we describe the artificial heart program since its beginning.

And next we describe how the resources are allocated to this program, which is only one of the many programs our institute sponsors.

We will discuss how we assess and give you the programs, and you might be interested to know, Mr. Chairman, that in the 22 years of existence of the program we have had nine full-fledged scientific figures, the last one being summarized in this report which has been given to the committee.

My statement also describes, discusses ethical considerations, alternatives to heart replacements and some aspect of risk and quality of life.

Of all these issues I would like to highlight a few points, and most importantly the evolution of the program since it was created some 22 years ago. And indeed, the program started in 1963, under Congress' impetus, which, in fact, in 1964 decided to introduce a line in the budget of the Institute, and appropriated the specified amount of $600,000.

In the 1960's and early 1970's, some quite important milestones resulted from the program, not least was the development of the series of blood oxygenators, and the intraballoon, which are devices which are now part of everyday clinical care.

As well short-term circulatory assist devices were developed and have been used quite extensively, mostly in the support of patients in the postsurgical phase of their treatment.

In the early 1980's we focused our program on the development of components for the electrically powered ventricular assist system. And, of course, the Jarvik-7 artificial heart, which was discussed at length this morning, reached maturation, and moved from the developed model testing into clinical application.

As you know, five such total clinical replacements have been done with this device, and another, the temporary bridge-to-transplant application have been made using the Jarvik and other devices, as well.

Currently, we are testing some new devices. One is here, for instance, which eventually will become a fully implantable device, one which will be another single ventricle, or eventually fully implantable artificial heart.

Having described briefly the history of the program I would like to mention how we are allocating resources to it. As I said, the first allocation of the resources were made specifically for this instance, the artificial heart program.

But progress in 1964, since then the Institute's advisory process, which I will mention in a few minutes, has regularly allocated some amount of moneys each year from our regular appropriation. For instance, in 1967 this amount reached $8 million; in 1974, it reached about $12 million a year; and the same amount has been allocated to this program since, with an exception in 1976 when we were allocated as much as $15 million.

It may be of interest to you, Mr. Chairman, that three-quarters of this amount is given to investigators by way of contract; in other words, it is a program, targeted program of the Institute, and approximately one-quarter in reference to awards, grants to investigators who submit applications for us and are previewed through our peer review system.

Let me now briefly mention the process that we utilize to make the determinations with what amounts of money will be allocated to this program.

When it was first started most of the advice given to the Institute came from other consultants which were called in to provide advice and, again, ad hoc; a somewhat spotty fashion.

Since 1974, the Institute has greatly relied on a more formalized process which includes the cardiology advisory committee, the body of experts in cardiology and other disciplines which is advising the Institute for overall cardiology heart research of the program of the Institute, of which the heart program is only one component.

The advice of that body, the advisory cardiology committee, goes to the National Heart, Lung, and Blood Advisory Council, which is another body made up of the experts in the relative field, as well as lay individuals, leading, not scientific experts.

With all this advice that we receive, first from the cardiology advisory committee, and then from the national advisory council, the Director of the Institute makes a final decision as to the allocation to the various programs of the Institute.

I think it is important for me to emphasize that the Institute has many competing priorities. This morning when we started these hearings, some health statistics were given to you, and, indeed, about half of the deaths in this country each year are due to cardiovascular diseases. If we take all the diseases which are within the purview of our Institute, approximately 68 to 69 percent of all the deaths in this country are due to diseases which are within our purview.

I should say that, sir, with regard to this, there is a number of very significant spinoffs that have come from the artificial heart programs. I should mention a number of cardiovascular implants, the development of polyurethanes, an inert substance which is used in many prostheses and many other devices.

The collagen-derived artificial skin is also a spinoff of the program.

And finally, materials which are used for the fabrication of contact plants and other devices, are a spinoff of our program.

To conclude my remarks, Mr. Chairman, I would like to emphasize that the institute mission is to foster and support a broad range of activities designed to reduce deaths and disability. We estimate that as many as 20 to 30,000 Americans suffer each year from heart failure, with very few, if any at all, preoperative choices.

Our main goal is to prevent this condition from developing. But meanwhile, we feel that total heart replacement with a mechanical device has some potential to become a preoperative alternative.

And, therefore, we count on you to support some aspect of the experiment which Dr. DeVries so aptly described, which hopefully will demonstrate whether this preoperative choice has some value or not.

Thank you very much.

[The prepared statement of Dr. Claude Lenfant follows:]

Statement by

Claude Lenfant, M.D.
Director

National Heart, Lung, and Blood Institute

National Institutes of Health

on the

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
MECHANICAL CIRCULATORY SUPPORT PROGRAM

Committee on Science and Technology
Subcommittee on Investigations and Oversight
United States House of Representatives

February 5, 1986

Introduction

Mr. Chairman and members of the Committee, I am pleased to have this opportunity to speak to this Committee on the National Heart, Lung, and Blood Institute's (NHLBI) Artificial Heart Program.

Since 1964, the NHLBI has fostered the development of a family of devices to assist or replace the failing heart or lung. Various types of mechanical circulatory support are required to treat the spectrum of cardiac dysfunctions attributable to advanced heart disease.

I would like to categorize the family of devices developed under the stimulus of the Institute's Artificial Heart Program into two main areas: (1) mechanical devices, such as a ventricular assist device or intra-aortic balloons, that function in concert with, and as an aid to, the natural heart that remains in place, and (2) the artificial heart, a biventricular mechanical device, that supports the circulation after removal of the natural heart. Both types of mechanical circulatory support devices will be discussed during my presentation.

Heart failure can be regarded as a failure of the pumping action of the heart to deliver blood in quantities sufficient to sustain organ function. The causes are many and include coronary heart disease, heart muscle disease, high blood pressure, and deformed heart valves. Patients who progress to this stage of heart disease experience severe shortness of breath, swollen extremities, confinement to a bed-to-chair existence, and premature death. It is the Institute's belief that in the future many of these patients might be returned to a better quality of life by means of some form of mechanical assist or replacement of the failing heart.

During its 20-year history, the Program has seen sustained progress, based on an orderly sequence of developments and the resolution of many scientific problems leading to the fabrication of prototype devices and subsequent clinical evaluation of the most promising concepts. As a result, several devices have emerged, each having a limited range of applicability and each representing a further refinement in the technology. Investigations continue towards our ultimate goal, the development of an untethered, implantable artificial heart.

I must emphasize that the only available therapy today for patients with end-stage or irreversible heart failure is cardiac transplantation. This strategy has limited applicability because of the scarcity of heart donors. The Institute, therefore, supports continued research and development of the artificial heart, with cautious optimism for its success, and with the belief that costs may be balanced by benefits.

Description of the Artificial Heart Program

I will now briefly review for you the history of the artificial heart program and mention in passing some of the milestones achieved en route. In my introduction, I alluded to a family of devices. These are the result of sustained methodical development that has been pursued for more than two decades. In 1963, the impetus for a government-supported artificial heart program originated in the Congress. The program was subsequently endorsed by the National Heart Advisory Council, and in July 1964, the Artificial Heart Program was established within the Institute.

In 1964, the enabling legislation provided $581,000 to create the Artificial Heart Program. Since then, the NHLBI has provided approximately $218 million of support for the constituent research areas that comprise the artificial heart program. Since 1969, the annual expenditure of the Artificial Heart Program has averaged approximately $10-15 million for support of grant and contract research.

During the late 1960s and early 1970s, while pursuing the goal of an artificial heart, worthwhile milestones were reached. These included devices or components such as the intra-aortic balloon pump, blood oxygenators, air-driven circulatory support devices, implantable pressure transducers, and blood flowmeters. The intra-aortic balloon pump is today an important component used in everyday clinical care for maintenance of blood circulation in patients with circulatory collapse following cardiac surgery.

Another important resource developed by the Artificial Heart Program is a community of basic scientists, engineers, and clinicians with their expertise and interest committed to the substantial research problems posed by the artificial heart such as the biologic interface (or what happens when blood meets artificial surfaces), engine miniaturization, blood pumps, energy transmission methods, and physiologic effects.

During this time, short-term circulatory assist devices, which maintain the circulation for several days or weeks, were developed to the point where they underwent, between 1974 and 1979, clinical evaluation in selected patients. These studies demonstrated that the devices could be safely used in patients with severe, reversible, ventricular dysfunction following cardiac surgery or myocardial infarction. Better than 25% of these patients, who would otherwise have died, have had a useful long-term survival.

In the early 1980s, there was significant progress on a number of fronts. Primarily, the NHLBI Program was directed towards the integration of developed components into a tether-free, electrically powered ventricular assist system capable of functioning in humans for a period of two years without mechanical failure. In addition, the pneumatically actuated Jarvik-7 artificial heart, a product of NHLBI support to the University of Utah, has entered into clinical investigation and into the private sector.

Five patients have received the Jarvik-7 for permanent circulatory support. Two patients are alive 14 months and 11.5 months after implant. Twenty-one patients have received mechanical circulatory support as a bridge to cardiac transplantation, 7 received artificial heart replacement devices, 12 had support with ventricular assist devices, and 2 were supported with a membrane oxygenator. Ten patients have been successfully transplanted with human hearts and, as of January 27, 1986, two patients of these ten were stable on circulatory support awaiting a donor heart. Two patients have a 17-month survival with a quality of life comparable to other heart recipients. Of note, the longest surviving bridge patient was supported with an implantable electrically powered ventricular assist device.

Currently, the Institute supports reliability testing of fully implantable electrically powered ventricular assist systems. The purpose of this "Device Readiness" Program is to insure device mechanical integrity, safety, and performance in animals before beginning clinical evaluation in 1988.

Different systems also under development are powered by thermal energy from an implanted thermal storage unit. The fully implantable thermally powered ventricular assist system, which is being readied for clinical evaluation in the early 1990s, will afford the potential for the most compact system and a lifetime of 5-10 years.

Research on untethered, implantable artificial heart devices has been supported by investigator-initiated grants. Recent progress in the laboratory and in animals has paved the way for an NHLBI targeted program for developing fully implantable electrically powered biventricular assist and total artificial heart systems. The program will begin in 1987 and follow the sequence previously established for the ventricular assist devices, of validation through bench and animal testing, followed by clinical evaluation.

Allocation of Resources

In the first year of the Artificial Heart Program, $661,000 was contracted for study of the need and technical feasibility. In 1967, over $8 million were contracted in over a dozen program areas to test the feasibility of various design concepts. Since that time, targeted contract funding has remained stable between $8-12 million.

In the early years of the Program, allocation of resources was based upon recommendations of ad hoc consultants during periodic reviews. In 1974, the substantial involvement of a permanent external advisory group, the Cardiology Advisory Committee was developed. The Committee advises and assists in the scientific design and review of current programs in the areas of cardiac diseases, cardiovascular diseases, and relevant technological developments. This Committee of experts in cardiology, cardiovascular surgery, basic science, biomathematics, and biomedical engineering completed a major review of the Artificial Heart Program in 1977 and has continued a systematic, ongoing review of program activities since that time.

Secondary concept review of all ongoing and proposed programs is provided by the NHLBI Advisory Council, which recommends areas of research to be supported by contracts and the percentage of the budget to be expended by contracts. Final decisions on the allocation of resources for artificial heart research are based on the competing priorities of all the heart, lung, and blood disease research programs supported by the NHLBI.

The targeted NHLBI program has supported $187 million in research, development, and clinical evaluation of mechanical circulatory support devices. Over $56 million has focused on the development of several implantable miniature engines, the smallest of which is about the size of a C-cell battery. Thirty-one million dollars have supported testing and evaluation of the many developments that have evolved from the programs, while, coincidentally, another $31 million has gone into biomaterials research.

While there remain many unanswered questions regarding the interaction of biomaterials with blood and other tissues, it is interesting to note several biomaterial developments which have resulted as a direct or indirect result of work supported by the Artificial Heart Program, for example, collagen-derived artificial skin, cardiovascular implants, polyurethane--durable materials with good blood compatibility--and multifunctional materials which have been used in contact and intraocular lenses. Similar developments are identifiable for other program areas.

In conjunction with the targeted program, the Institute has supported $30 million in investigator-initiated grants, primarily on artificial heart research. Completion of the Program will probably require support through the 1990s, after which, completion of the transition of the Program to private industry is planned.

Program Assessment

From the inception of the Artificial Heart Program, the NHLBI has been keenly aware that the development and clinical application of the artificial heart would elicit a broad range of questions and issues. Thus, from the beginning, the NHLBI has sponsored periodic reviews of both technical and nontechnical issues including the social, ethical, economic, and other issues related to artificial heart devices. There have been nine review panels composed largely of nonfederal consultants whose research interests reside outside the Artificial Heart Program.

Most recently (1983), an ad hoc Working Group on Mechanical Circulatory Support was established to develop an overview of the Artificial Heart Program and advise the NHLBI on issues, activities, and policies relevant to the investigational and anticipated therapeutic use of such devices. Their report (1985) addresses program direction, needs, and costs as well as societal and ethical issues. The Working Group estimated that there would be approximately 17,000 to 35,000 medically eligible candidates annually for the artificial heart. The group also estimated that the costs of the initial implantation and an average four and one-half year follow-up would be approximately $150,000 (1983 dollars). Thus, the gross annual cost to society for 17,000 to 35,000 implants per year could be in the range of $2.5-5.0 billion. These costs are comparable to costs incurred during the treatment of patients with severe burns, some types of cancer, and similar to recent estimates regarding the costs of treating patients with AIDS. Thus, the cost of the artificial heart will likely fall within the broad range of currently accepted, expensive medical procedures.

Ethical Considerations

The Working Group (1985) evaluated the ethical considerations for clinical investigation of mechanical circulatory support devices and offered the following guiding principles:

1. The research design should be sound, and there should be adequate preclinical testing of the mechanical devices before they are used in humans.

2. The physician-investigators should be competent not only to perform the research but also to provide good medical care of the patient-subjects and to minimize risks.

3. There should be a favorable balance of risks and anticipated benefits.

4. There should be informed consent in discussions involving the patient-subject, physician-investigator, and others.

5. There should be equitable selection of subjects and patients.

6. There should be compensation for research-induced injury.

The Working Group further commented that the use of these devices in their earliest phase should be viewed as innovative medical practice and the device as investigational. Investigative plans to use these devices should be reviewed by Institutional Review Boards (IRBs) according to standards established in relevant regulations of the Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA).

Alternatives

The Working Group (1985) reaffirmed that current medical management for patients with end-stage heart disease is not effective. They noted that the only alternative therapy is heart transplantation, which is limited by donor availability.

Clearly the best means of disease control is prevention, and this can only come with better understanding of the biology and pathobiology underlying the various heart diseases that lead ultimately to heart failure. Much progress in prevention of heart disease already has been made as evidenced by the continued decline in these diseases over the past two decades. However, the incidence and prevalence of heart failure remains high and is in need of control through continued investigation.

Risk and Quality of Life

It is hoped that within two to three years, implantable long-term assist devices will be available which will provide two years of reasonably good quality of life. Although this is an intermediate goal, with further development, at least five years of life can be expected. It is anticipated that the recipients will be able to engage in most normal ambulatory activities and some forms of moderate exercise. But even under the best of circumstances, the patient will have an awareness of the device. Medication and daily exchange of batteries will be required. Current research efforts are being focused on prevention of potential complications such as blood clotting, the risk of stroke, and infection.

At present, there is no way to predict with any certainty the quality of life for a recipient of an artificial heart. Heart transplantation patients are perhaps the closest parallel, and data from these patients suggest that quality of life is quite acceptable. Let me reemphasize that patient-candidates qualifying for heart transplant have an average life expectancy of 6-12 months and a bed-to-chair existence with medical therapy alone.

Summary

The NHLBI supports a broad range of activities designed to reduce death and disability from heart disease. Our primary efforts have been and will be to improve our fundamental understanding of these diseases, their control, and ultimate prevention. Technical progress suggests that implantable, safe, and effective artificial heart devices, reliable for several years, are feasible. It is a reasonable assumption that these devices may provide an extended lifetime of acceptable quality. The Institute will continue its policy of reassessing the artificial heart program in light of new knowledge. With these perspectives in mind and in view of other research opportunities, we hope to allocate stable and reasonable support to complete the development and clinical evaluation of the artificial heart. The potential to relieve the suffering of patients who have severe congestive heart failure makes this effort worthwhile.

This concludes my statement. I will be pleased to answer any questions.

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Director, National Heart, Lung,
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October 12, 1928, Paris, France

Education: B.S., University of Rennes, France, 1948. M.D., University of Paris, France, 1956.

Professional History: 1957-1958, Research Fellow, University of Buffalo, New York. 1958-1959, Research Fellow, Columbia University, New York. 1959-1960, Assistant Professor of Physiology, University of Lille, France. 1961-1965, Clinical Instructor of Medicine and of Physiology and Biophysics, University of Washington, Seattle. 1966-1967, Clinical Assistant Professor of Medicine and of Physiology and Biophysics, University of Washington, Seattle. 1968-1971, Associate Professor of Medicine and Physiology and Biophysics, University of Washington, Seattle. 1970-1972, Acting Associate Director, Collaborative R&D Program, National Heart and Lung Institute, NIH. 1970-1972, Associate Director for Lung Programs, National Heart and Lung Institute, NIH. 1971-1972, Professor of Medicine and Physiology and Biophysics, University of Washington, Seattle. 1972-1980, Director, Division of Lung Diseases, National Heart, Lung, and Blood Institute, NIH. 1981-1982, Associate Director for International Research, NIH. 1981-1982, Director, Fogarty International Center for Advanced Study in the Health Sciences, NIH. 1982-Present, Director, National Heart, Lung, and Blood Institute, NIH.

Professional Organizations: Association of American Physicians, American Society for Clinical Investigation, American Physiological Society, American Federation for Clinical Research, French Physiological Society, International Federation for Medical Electronics, American Society of Zoologists, Society for Experimental Medicine and Biology, Undersea Medical Society, New York Academy of Science.

Honors, Awards: Thesis Prize, University of Paris, France, 1956. Commendation Tohoku Medical Society, Sendai, Japan, 1973. Superior Service Honor Award, DHHS, 1974. Regents' Professor, University of California, Los Angeles, 1975. Testimonial Dinner, American Thoracic Society, 1979. Honorary Fellow, American College of Chest Physicians, 1979. Honorary Professor, National Yang-Ming Medical College Taipei, Taiwan, 1980. Honorary Professor, Universidad Peruana Cayetano Heredia, Lima, Peru, 1981. Senior Executive Service Performance Award, 1982. Elected Institute of Medicine, National Academy of Sciences, 1983. American Heart Association Scientific Councils' "Distinguished Achievement Award," 1983. Senior Executive Service Performance Award, 1983. Honorary Fellow - Council on Clinical Cardiology - American Heart Association, 1984. Senior Executive Service Performance Award, 1984. Forrest M. Bird Contributory Award, American Respiratory Therapy Foundation, 1985. Senior Executive Service Performance Award, 1985.

Authorship, Editorship: Author or Co-Author of 192 scientific publications Served on Editorial Boards of: Am. Journal of Physiology; Journal of Applied Physiology; Respiratory Physiology; Am. Review of Respiratory Disease; Undersea Biomedical Research; Proceedings of Society for Experimental Biology and Medicine; Revue Francaise des Maladies Respiratories; Journal of Applied Physiology; Respiration, Environmental and Exercise Physiology; Am. Journal Am. Journal of Medicine; Continuing Education for Family Physicians; Executive Editor of 38 volume monograph series, Lung Biology in Health and Disease.

Mr. **Volkmer**. Thank you very much, Dr. Lenfant.

Mr. Norris.

Mr. **Norris**. Yes, Mr. Chairman. Thank you for the opportunity of representing the Food and Drug Administration before your subcommittee.

Dr. Mohan, on my right, is head of FDA's Office of Device Evaluation, which is part of our Center for Devices and Radiological Health, headed by Dr. John Villforth.

On my left is Dr. Charles McIntosh, who is Chairman of FDA's Circulatory System Devices Advisory Panel.

I will present a summary of FDA's testimony. Dr. McIntosh will speak on behalf of FDA's panel, advisory panel.

Without question, total artificial heart implants have the potential of creating a dramatic breakthrough in medical therapy. In the series of artificial heart implants, both as permanent or chronic organ replacements and as temporary or bridge implants used until human donor hearts can be found, has generated enormous public interest, and has commanded front page headlines since December 1982, when the first Jarvik-7 heart was implanted.

Before I begin my testimony in earnest I would like to spend 2 of my 10 minutes just giving you a brief background of the context in which these issues are arising.

Several of the witnesses that have preceded me have given some of this information, but I just want to summarize in a couple of charts very briefly, and we will submit the charts as part of our testimony.

First of all, as I know you are aware, our congressional—our authority and responsibility to regulate in this area was created by Congress in 1976 as part of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act.

Before the 1976 amendments, our authority and responsibility was only to do a retrospective review of marketed devices. And what we were given by way of 1976 amendments was prospective as well as retrospective authority and responsibility.

We have been accomplishing this through a process which is—is alleged to be cumbersome. I would suggest to you that I think it is a well-balanced process. The amendments recognize the range of risk posed by the wide variety of medical products and how they are used. And it prescribes a tiered system of regulation which is proportional to those risks. Thus, the greater the risk, the greater the level of regulation.

For critical care and life sustaining devices, such as the artificial heart, the law imposes the most stringent set of regulatory requirements.

Essentially, prospective manufacturers must seek marketing approval from FDA based on a proof of product safety and effectiveness. Safety and effectiveness are what are critical here.

In the first chart (chart 1), it is indicated that for devices manufactured after the medical device law was enacted in 1976, the pathway to securing a PMA or premarket approval involves several steps.

IDEs FOR EXPERIMENTAL HEART IMPLANT DEVICES: SPECIFIC FACTORS FDA REQUIRED

- Preclinical studies were adequate (toxicity, design, durability)
- Research goals were achievable
- Safety and effectivness information could be derived
- Patients' rights were safeguarded
- Only terminal cases were included
- Surgical and engineering qualifications were adequate
- Long-term commitment to patient care was made

CHART 1

The first step is for the company to, on its own initiative, do preclinical animal and laboratory testing. And then they come to the FDA once they have done what they believe to be a satisfactory job of the preclinical animal and laboratory testing, and obtain, or request from us, what is called an IDE—investigational device exemption.

The chart here (chart 2) lays out very briefly the contents of what an IDE for an experimental device such as an artificial heart would require. Some of the information that is required is very detailed, some of it is very simplistic.

CONTENTS OF AN IDE FOR AN EXPERIMENTAL DEVICE

- Background on sponsor
- Report of prior investigations (e.g. animal and lab testing)
- Summary of investigation plan
    - — Purpose
    - — Protocol
    - — Risk analysis
    - — Description of device
    - — Monitoring procedures
    - — Labeling
- Description of manufacturing methods, facilities, and controls
- Research agreement between the sponsor and sponsor's certified investigators
- List of reviewing IRBs and actions
- Informed consent materials

CHART 2

The background of a sponsor, for example, is just a very brief summary of the background. The report on the prior investigations goes into some of the detail of the work they have already completed.

They probably have already prepared by that point a summary of their investigation and results to that point, anyway——

Finally, or next, a summary of their investigation plan is required. The chart lays out some of the elements of that.

Next, a description of their manufacturing methods, and the facilities and controls they intend to employ in the IDE phase of their work.

Finally, the research agreement between the sponsor and the sponsor's certified investigators, and a list of reviewing IRB's and actions.

And finally, and not least, certainly, the informed consent materials that were required of patients before the experiment would proceed.

Next, if I could have the third chart (chart 3), I have laid out here very briefly, and we have had some testimony today on the artificial hearts to date that have been implanted under IDE's.

EXPERIMENTAL HEART IMPLANT DEVICES IDEs GRANTED BY FDA (as of 2/3/86)

Model/Indication	Institution/Investigator	Maximum No. of Implants Permitted	Recipients/Length of Implant
JARVIK-7 (100 cc) • Permanent ("chronic")	Humana Hospital (Dr. DeVries)	7	— Pt. 1, died 111 days — Pt. 2, alive 434 days — Pt. 3, alive 450 days — Pt. 4, died 10 days
JARVIK-7 (100cc) • Temporary ("bridge")	1. Univ of Pitt. (Dr. Griffith)	10	— Pt. 1, human heart transplanted after 4 days, currently alive — Pt. 2, alive after 1 day
	2. Univ. of Ariz. (Dr. Copeland)	10	— Pt., human heart transplanted after 9 days; currently alive
	3. Abbott-Northwestern Hospital (Dr. Joyce)	10	
PENN STATE HEART • Temporary ("bridge")	Penn State Univ. Hershey Medical Center (Dr. Pierce)	7	— Pt., human heart transplanted after 10 days, died

CHART 3

As you can see from the chart, we have had 4 Jarvik-7, 100 cc heart implants, which are the largest in the permanent category. We have had four of those. And the status of the patients today is laid out; two are alive, and two have died.

Next, we have the institutions and the physicians involved in implanting the Jarvik-7 100 cc device as a temporary bridge, or what is called a bridge-to-implant. Again, the institutions are identified.

Each of the institutions enumerated there have been given authority for a maximum number of 10 implants before they have to come back to the Food and Drug Administration for authority to expand those implantations.

To date we have had two implanted at the first institution, the University of Pittsburgh; and we have had one implanted at the University of Arizona.

The next line just indicates that there is another heart available that is called the Penn State heart. And that is authorized for a temporary bridge implantation as well.

To date, one of those has been implanted.

If we could call up the fourth chart here (chart 4), in granting an IDE the FDA must be satisfied that all elements of the clinical studies proposed by the sponsors are scientifically sound, and that the study protocols contain safeguards that will adequately protect those who are involved in the studies.

OTHER RECENT ARTIFICIAL HEART IMPLANTS
(As of 2/4/86)

Model/Indication	Institution/Investigator	No. of Patients	Recipients/Length of Implant
JARVIK-7 • Permanent (100cc) ("chronic")	Karolinska Institute Sweden (Dr. Sembe)	1	— Pt., died after approx., 210 days
JARVIK-7 • Temporary (70cc) ("Bridge")	Abbott-Northwestern Hospital (Dr. Joyce)	1	— Pt., transplanted after 45 days, alive
	Univ. of Ariz. (Dr. Copeland)	1	— Pt., alive after 1 day
PHOENIX HEART • Temporary ("Bridge")	Univ. of Ariz. (Dr. Copeland)	1	— Pt., transplanted after 11 hrs., died

CHART 4

As the fourth chart indicates, IDE's for experimental heart implant devices—and I will emphasize experimental in that terminology—we require a number of specific factors.

We looked in great depth to see that the preclinical studies were adequate. And in addition, research goals must be achievable.

We don't want to, and did not want to want this to go forward without a critical review of that achievability of the research goals.

Safety and effectiveness, as I pointed out earlier, we are required by statute to review. Patient rights, the safeguarding of the patient's rights is a critical issue.

In addition, as has been pointed out by various witnesses, only terminal cases were permitted to be included under the IDE's. Surgical and engineering qualifications had to be adequate.

And finally, long-term commitment of care had to be made.

Now, as was pointed out by some of the earlier witnesses, this becomes particularly critical as we become more and more involved in the bridge transplants because, in fact, some of the bridge transplants may turn out to be de facto permanent.

And if a person has implantation, and the institution is not prepared to take on a permanent transplant patient, then we are going to have a problem. Now, once we were certain that these criteria had satisfactorily been met, the next question we confronted was how many implants should be permitted.

On one hand, because of the newness of the concept and the potential for significant postoperative trauma, we felt compelled to limit the number of patients in this investigation more severely than normal.

On the other hand, we wanted to allow the investigator a full opportunity to accumulate sufficient experience and data about the performance of the device, to permit him and us to arrive at some reasonable conclusions about its safety and effectiveness. We also wanted him to have enough patients in the study so that he could identify trends and make midcourse corrections as necessary as he went along.

Based on these considerations we decided on seven as a reasonable number of patients for the permanent implantation series.

From this point onward our role was to watch over the study, through review of required periodic reports from the company. We have thus far had occasion to intervene three times during the study in response to problems that arose.

First, when a valve in Dr. Clark's heart fractured we approved a change in the protocol that was proposed by the sponsor to allow the use of another valve type in subsequent hearts.

Second, in order to improve the chances of survival we approved a change in the study protocol which shortened the mandatory waiting period between the identification of a candidate and the implant. This change was also proposed by the sponsor based on the experience with Dr. Clark.

Third, after observing a trend involving strokes and other complications in the three recipients following Dr. Clark, we imposed additional restrictions on the investigation.

Let me now describe this latter action in a bit more detail.

It was clear by the summer of last year that although the device was obviously capable of prolonging life, strokes and kidney damage were two of the major complications for recipients of the Jarvik-7 heart.

By that time, three of the four American patients had experienced seizures and strokes, and all of them had experienced kidney damage, bleeding, and anemia.

Let me emphasize at this point that these were not unanticipated effects. We knew about their possibility from the preclinical animal studies.

What concerned us was the severity of the effects, and the consistency with which they were occurring. A major question was, and still is, whether these complications are inevitable with this particular model, or whether they can be prevented or ameliorated by changes in patient management.

In light of these questions, we requested from the company, a detailed report on the clinical management and outcome for all of the implant recipients to date.

Upon receipt we shared this information with our Circulatory System Devices Advisory Panel, comprised of outside experts in the field of cardiology and cardiac surgery. Based on the information presented in this report, we felt the panel should have the opportunity to meet directly with the manufacturer and with Dr. William DeVries, in order to further discuss and to evaluate the clinical results up to that point.

This interchange took place during a specially convened meeting of the panel last December 20. As a result of these discussions the panel recommended, and FDA has agreed, that certain additional conditions should be imposed in the study. Dr. McIntosh will describe them in his testimony.

Let me just talk briefly now about the emergency use guidance that has come up a number of times today. Aside from approving and monitoring the clinical studies, FDA has had to consider the very difficult issues that arise from the emergency use of artificial hearts outside of any approved research protocols.

As you may know, an artificial heart not covered under an IDE was used as a temporary bridge implant in Tucson, AZ last year. Partly as a result of that incident, we have recently developed and issued guidelines covering the emergency use of such unapproved devices.

Briefly, the guidelines provide for a single use of an unapproved device in an emergency, life-threatening situation, without having first obtained an IDE from the FDA. Such a one-time use is permitted provided that, first, the emergency use can later be justified.

Second, the user-physician has tried to obtain an independent medical assessment from an uninvolved physician, informed consent from the patient, or if incompetent, from his guardian, and clearance from both the medical facility and the local IRB.

And third, the FDA is notified immediately afterward—and I will stress afterward there—not before, but afterward.

As the chart that is up there shows you, here a number of devices have been implanted without IDE prior approval. One was, of course, the Swedish implantation, and there was no real responsibility for the Swedish physician to obtain it from us; we list it there for continuity of information.

We have also, as was indicated in the testimony earlier, had two additional implantations during the last couple of days. On February 3, of this year, a Jarvik-7, 100 cc bridge device was implanted at the Texas Heart Institute, by Dr. Cooley, on an emergency, one-time approval basis. And in addition, at the University of Arizona, Dr. Copeland implanted a Jarvik-7 bridge device of a 70 cc, or small Jarvik bridge device, on February 2.

In establishing these guidelines our goal was to protect patients against the widespread use of untested devices, while at the same time allowing for legitimate emergency use for the benefit of the patient, when circumstances require it, for example, while the IDE is being filed or considered.

A key point is that we cannot allow the continued use of a device whose performance is unknown, even in an emergency, without the prompt analysis of data and maximum concern for patient safety. While FDA does not intend to interfere in emergency patient care situations, we want to guard against a situation in which a user could stockpile untested devices and bypass the normal process through which investigational products are proven safe and effective, possibly exposing by that stockpiling methodology, patients to unwarranted risk.

Once the single allowable emergency use has occurred, we believe it is reasonable that users would be able to anticipate the vast majority of potential future uses and needs for the device. Therefore, the guidelines prohibit the manufacturer from shipping more devices to potential users until we have approved a clinical investigation.

I should note here that we are required to act by law on an application for an IDE within 30 days of its submission.

A case in point is the recent implant of the smaller size version of the Jarvik-7 heart in a young woman in Minneapolis. As I indicated earlier, this device is not under an IDE. Its one-time, emergency use, did conform to the guidelines, and we have notified the manufacturer that an IDE must be granted before the small heart may be used again, absent an extraordinary situation.

A second emergency implantation of the 70-cc heart was done at Tucson with FDA's knowledge 3 days ago. That implantation took place with both our knowledge and our consent. We obtained the advice of our advisory panel. In this case the manufacturer and the physician contacted us in advance of the implantation and, based on the success to date of that particular device we were willing to authorize its use.

In closing, Mr. Chairman, I want to stress that the opportunities and problems surrounding the experimental use of the artificial heart dramatically illustrate the situation we face in regulating new medical technologies.

Under such situations, we are required to carefully balance competing worthwhile goals in order to ensure prompt availability of new safe and effective therapies while maintaining needed safeguards for patients and research subjects.

Let me emphasize, too, what often is forgotten in the excitement surrounding dramatic new technologies. This is very preliminary research not unlike a phase 1 drug study, and its purpose is to explore essential but preliminary human knowledge. The device, simply put, is experimental.

In summary, the first of our goals is to bring to the patients valuable new products that can enhance and prolong life, and to do so with as little delay as possible.

Examples of such breakthrough devices which recently have been approved by the FDA are:

The magnetic resonance imaging device, which gives clinicians a window into the human body, without surgical intervention;

Second, the implantable defibrillator, which corrects life-threatening rhythm disturbances of the heart and provides instantaneous, life-saving resuscitation;

Third, the cochlear implant, which aids the profoundly deaf;

And fourth, the lithotripter, which relieves the agonizing pain associated with kidney stones without the trauma and costs of surgery.

In this aspect of our role, we act as a guardian of patient safety while still serving as a facilitator, a conduit through which new products are brought to market in a timely, orderly, and properly accountable fashion.

Our second goal is to assure that human trials of new devices are conducted only on products with demonstrated promise, that they are carried out using good science in a well-defined and limited study population, and that the rights of patients to be fully informed about the risks of participating in these trials are adequately protected.

Once the clinical trials are over, we have to be convinced that the evidence does indeed indicate that the device is safe and effective before we allow it to be marketed.

There is a dynamic and very delicate balance between these two goals, in which FDA as the protector of the patient is called upon to act both as an accelerator pedal and as a brake pedal. To reconcile them requires good judgment, as well as good science.

We must do the best we can to avoid holding up new technologies, while at the same time being careful not to allow patients to be used in premature or ill-advised clinical trials. In the case of the artificial heart, we imposed certain restrictions to assure the scientific integrity of the study, yet we recognized the need for some freedom on the part of the investigator to gather the kind of data needed to determine the viability of the device.

We have also understood that it is not our role to intervene in medical practice. We have not stationed ourselves in the operating room.

But as needed, we have interceded at various points in the study to ensure that, if appropriate, course corrections were made.

Another general problem that the artificial heart exemplifies is that we must often make decisions of major importance based on less-than-perfect information. For example, is there something intrinsic about the Jarvik-7 heart that makes strokes highly likely? Or can changes in patient management or minor changes in design mitigate the problems?

No one really knows at this point, and so, balancing the potential benefits and risks very carefully, we will proceed, but with caution.

Thank you, Mr. Chairman, this concludes my statement.

I would be pleased to answer any questions.

[The prepared statement of John A. Norris follows:]

STATEMENT

BY

JOHN A. NORRIS, J.D., M.B.A.

DEPUTY COMMISSIONER OF FOOD AND DRUGS

FOOD AND DRUG ADMINISTRATION

U.S. PUBLIC HEALTH SERVICE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

COMMITTEE ON SCIENCE AND TECHNOLOGY

February 5, 1986

FOR RELEASE ONLY UPON DELIVERY

Mr. Chairman:

I very much appreciate having the opportunity to participate in this morning's hearing on the use of artificial heart implants and to discuss with you the role of the Food and Drug Administration (FDA) in regulating this new technology. With me today is Dr. Kshitij Mohan from our Center for Devices and Radiological Health, which is the operational arm of FDA responsible for medical devices. Dr. Mohan heads up the Center's Office of Device Evaluation, which is charged with the responsibility of evaluating and approving new products, including cardiovascular devices such as the artificial heart.

Without question, total artificial heart implants have the potential of creating a dramatic breakthrough in medical therapy. The series of artificial heart implants, both as permanent organ replacements and as temporary implants used until human donor hearts can be found (so-called "bridge-to-transplants"), has generated enormous public interest and has commanded front-page headlines since December 1982, when the first Jarvik-7 heart was implanted.

In my testimony today, I will outline the responsibilities of the FDA in overseeing and approving the development and marketing of medical devices generally, and how we have carried out these responsibilities in the case of the artificial heart. I will summarize the events leading up to FDA's decision to allow human trials of the total artificial heart in humans, as well as the rationale underlying our decision and the conditions we have imposed on this research. I will then update the Subcommittee on several recent events associated with the clinical trials involving the Jarvik-7 heart at Humana Hospital. I will also review how we at FDA are attempting to ensure that new, unapproved products such as the artificial heart may be used outside of a research protocol during emergencies without subverting the safeguards for the benefit of patients that we normally impose on experimental use in humans of unapproved products.

FDA REGULATION OF MEDICAL DEVICES

Let me begin with a brief overview of the mechanisms we use in regulating medical devices, and the legal authority that underpins those mechanisms. In 1976, the Congress enacted the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act in an effort to protect the public further from hazardous and ineffective medical products. Up to that point, FDA's regulatory authority in the medical devices area had been limited to its taking action only after a device was in commercial distribution and was shown to be unsafe. This was changed by the 1976 Amendments. To a great extent, the framework of the 1976 Device Amendments was modeled after the basic approach we have used for many years in regulating drugs -- that is, a framework where we evaluate the safety and efficacy of the product before it can be marketed and where we monitor its performance once it is made available to clinicians and consumers. The Amendments also recognize the range of risks posed by the wide variety of medical products and how they are used, and it prescribes a tiered system of regulation which is proportional to those risks. Thus, the greater the risks, the greater the level of regulation.

For critical care and life-sustaining devices, such as the artificial heart, the law imposes the most stringent set of regulatory requirements. Essentially, prospective manufacturers must seek marketing approval from FDA based on proof of product safety and effectiveness.

For devices manufactured after the medical device law was enacted in 1976, the pathway to securing "premarket approval" involves several steps. The first step involves preclinical testing by the manufacturer to determine whether a new device performs according to technical specifications and meets specified scientific criteria. Preclinical work can entail laboratory as well as animal testing, and does not require any preclearance by FDA. Based on the body of preclinical evidence amassed from such tests, a manufacturer may then attempt to initiate the next phase -- human or "clinical" studies.

Before beginning these clinical studies, the manufacturer must first successfully recruit appropriate numbers and kinds of clinical investigators and secure approval of its proposed human studies from a local Institutional Review Board, or "IRB" -- a review group charged with reviewing the technical and ethical aspects of the study. If the

IRB determines that the device under investigation presents a "non-significant risk" to patients and that adequate informed consent can and will be obtained, the manufacturer need not obtain FDA approval to conduct human testing. However, if an IRB decides that the investigation would present a significant risk, the manufacturer must formally apply to FDA and receive the Agency's permission to commence clinical studies. (This permission is known as an Investigational Device Exemption, or "IDE," because it exempts the manufacturer from the statutory prohibition and associated penalties against shipping an unapproved device in interstate commerce.)

FDA's approvals of IDEs are based on extensive review of the firm's study protocol by FDA staff, sometimes in consultation with advisory panels of outside experts. Among other things, the protocol must contain the following information: (1) the scientific and medical objectives of the clinical testing; (2) the size of the study population needed to yield statistically valid evidence of the device's safety and effectiveness; (3) patient followup and data collection and analysis methods to be used; (4) the identity of the clinical investigators and investigational sites; and (5) assurances given to FDA that patients in the study will understand both the benefits and risks of participation via informed consent. Only when we are satisfied with the soundness of the clinical protocol, do we then authorize the manufacturer or "sponsor" to begin human testing.

Upon completion of clinical studies, a manufacturer who wishes to obtain marketing approval must assemble all the patient and device performance data developed during premarket studies into a premarket approval application, or "PMA." In conjunction with an advisory panel comprised of outside experts in the appropriate medical speciality, FDA reviewers evaluate the company's data to determine if the subject device has been shown to perform in a reasonably safe and effective manner and in accordance with its labeled medical claims. If the product and accompanying performance data withstand this scrutiny by FDA and our panel of medical experts, formal marketing approval is granted. Should the manufacturer wish to make significant changes in the device, either during the clinical investigation phase or after it has been approved for marketing, he must submit to FDA a supplement to the IDE or to the PMA application detailing the proposed changes.

HISTORY OF THE ARTIFICIAL HEART IDEs

We have granted IDEs for human studies with two models of total implantable artificial hearts: the Jarvik-7, manufactured by Symbion, Inc., and the "Penn State heart," developed at the Pennsylvania State University Medical Center at Hershey. The IDEs for the Jarvik-7 heart permit human studies for two investigational purposes: as a permanent replacement for a human heart, and as a temporary implant (bridge), to be used in patients who are awaiting the availability of a human donor heart. The IDE for the "Penn State heart" permits investigation as a temporary implant (bridge) only. It has been implanted thus far in one patient for this purpose.

The IDE for the Jarvik-7 artificial heart, which we granted to Kolff Associates (later Symbion, Inc.) in 1981, specifies Dr. William DeVries as the implanting surgeon, and limits the series of implants to seven patients. The first implantation under this IDE was performed on Dr. Barney Clark in 1982. As is well known by this time, three other United States patients have subsequently received permanent artificial Jarvik-7 hearts under this investigational protocol.

In addition, last year we approved three medical centers in this country to perform clinical studies on the use of the Jarvik-7 heart as a temporary bridge-to-transplant. To date, three of these procedures have been performed, the most recent being made just four days ago in Pittsburgh. Also, a new, smaller-sized version of the Jarvik heart has now been developed. Although an IDE has not been approved for the implantation of this smaller heart, it has been implanted in one case under FDA's emergency guidance which I will discuss later in my testimony.

In granting an IDE, FDA must be satisfied that all elements of the clinical studies proposed by the sponsors are scientifically sound and that the study protocals contain safeguards that will adequately protect those who are involved in the studies. In the case of the IDE for the Jarvik-7 heart, we began our review by evaluating the design and engineering characteristics of the device using the company's bench testing and animal data. At that stage, we wanted to be sure that the materials proposed for use in the device were not toxic and would reasonably be compatible with the body's internal environment. Another major concern at that stage was the adequacy of the device's hemodynamics -- that is, the device's ability to pump blood without undue turbulence or damage to blood cells. Finally, we also carefully examined the ability of the device to function in a biological environment over a long period of time without breakdown of vital components, such as the valves.

As is the case with virtually every drug or device, animal testing cannot fully predict the safety or effectiveness of a product in humans. Thus, the next step, once we were convinced that laboratory and animal testing had been satisfactory, was to review the company's proposed research protocol for clinical testing in humans. At this stage, we paid particular attention to the following factors:

1. Whether the research goals were clearly laid out and scientifically achievable, and whether the research would yield the type of information needed to support a claim of safety and effectiveness for this product.

2. Whether patients' rights were safeguarded by appropriate measures geared towards adequately informing them and their families about what to expect. For example, we wanted to be especially sure that patients and family members clearly understood the restrictions that would be imposed by having the recipient tethered to the large external drive system. In addition, we were careful to see that safeguards existed to insure that patients were made sufficiently aware of potential untoward events, such as strokes or kidney damage.

3. Whether, in selecting patients for the study, the sponsors had been careful to exclude those patients who might benefit from less experimental treatment, such as a human heart

transplant or drug therapy. The goal was to include in the study only those who had no other treatment recourse and were considered terminal. In other words, we did not want to subject patients to this experimental protocol who might benefit from other, more proven forms of therapy.

4. Whether the implant and patient management teams -- first at the University of Utah and later at the Humana Hospital -- possessed the specialized surgical and engineering qualifications to carry out the study.

5. Whether the hospital was prepared to make a long-term commitment to the care of these patients subsequent to their implantations.

Once we were certain that these criteria had satisfactorily been met, the next question we confronted was how many implants should be permitted. On one hand, because of the newness of this concept and of the potential for significant post-operative trauma, we felt compelled to limit the number of patients in this investigation more severely than normal. On the other hand, we wanted to allow the investigator a full opportunity to accumulate sufficient experience and data about the performance of the device to permit him and us to arrive at some reasonable conclusions about its safety and effectiveness. We also wanted him to have enough patients in the study so that he could identify trends and make mid-course corrections as necessary as he went along. Based on these considerations, we decided on seven as a reasonable number of patients for the series.

From this point onward, our role was to watch over the study through our review of required periodic reports from the company. We have thus far had occasion to intervene three times during the study in response to problems that arose. First, when a valve in Dr. Clark's heart fractured, we approved a change in the protocol that was proposed by the sponsor to allow use of another valve type in subsequent hearts. Second, in order to improve the chances of survival, we approved a change in the study protocol which shortened the mandatory waiting period between the identification of a candidate and the implant. This change was also proposed by the sponsor based on the experience with Dr. Clark. Third, after observing a trend involving strokes and other complications in the three recipients following Dr. Clark, we imposed additional restrictions on the investigation. Let me now describe this latter action in considerable detail.

RECENT DEVELOPMENTS

It was clear by the summer of last year that, although the device was obviously capable of prolonging life, strokes and kidney damage were two of the major complications for recipients of the Jarvik-7 heart. By that time, three of the four American patients had experienced seizures and strokes, and all of them had experienced kidney damage, bleeding, and anemia. Let me emphasize at this point that these were not unanticipated effects -- we knew about their possibility from the preclinical animal studies. What concerned us was the severity of the effects and the consistency with which they were occurring. A major question was, and still is, whether these complications are inevitable with this particular model, or whether they can be prevented or ameliorated by changes in patient management.

In light of these questions, we requested from the company a detailed report on the clinical management and outcome for all the implant recipients to date. Upon receipt, we shared this information with our Circulatory System Devices Advisory Panel, comprised of outside experts in the field of cardiology and cardiac surgery.

Based on the information presented in the report, we felt that the Panel should have the opportunity to meet directly with the manufacturer and with Dr. William DeVries, in order to further discuss and evaluate the clinical results up to that point. This interchange took place during a specially-convened meeting of the Panel last December 20. As a result of these discussions, the Panel recommended, and FDA has agreed, that certain additional conditions should be imposed on the study. These are as follows:

1. The FDA will assume a more direct oversight role as the clinical studies proceed, and will permit subsequent implants on a case-by-case basis. That is, approval for initiation of each of the remaining implants authorized by the IDE will be conditioned upon an analysis of data derived from the preceding implant.

2. The sponsor will submit to and have approved by FDA a revised IDE protocol, based on the experience gained with the last four patients. This protocol will include specific additional steps proposed by the surgical team at Humana Hospital to be taken in patient care and in data acquisition, including anti-coagulant therapy and pre- and post-operative drug and nutritional therapy. The revised protocol will

delineate changes in patient management and shall include, at a minimum, the addition of scientists with needed specialized medical and scientific expertise who will collaborate with Dr. DeVries.

3. The FDA will consult periodically with the Panel in carrying out these provisions.

EMERGENCY USE GUIDANCE

Aside from approving and monitoring the clinical studies, FDA has had to consider the very difficult issues that arise from the emergency use of artificial hearts outside of any approved research protocols. As you may know, an artificial heart not covered under an IDE was used as a temporary "bridge" implant in Tucson, Arizona, last year. Partly as a result of that incident, we have recently developed and issued guidance covering the emergency use of such unapproved devices.

Briefly, the guidance provides for a single use of an unapproved device in an emergency, life-threatening situation without having first obtained an IDE from FDA. Such one-time use is permitted, provided that: (1) the emergency use can later be justified; (2) the user-physician has tried to obtain an independent medical assessment from an uninvolved physician, informed consent from the patient or, if incompent, from his guardian, and clearance from both the medical facility and the local Institutional Review Board; and (3) the FDA is notified immediately afterwards.

In establishing this guidance, our goal was to protect patients against the widespread use of untested devices, while at the same time allowing for legitimate emergency use, for the benefit of the patient, when circumstances require it -- for example, while the IDE is being filed or considered. A key point is that we cannot allow the continued use of a device whose performance is unknown, even in an emergency, without the prompt analysis of data and maximum concern for patient safety. While FDA does not intend to interfere in emergency patient care situations, we want to guard against a situation in which a user could "stockpile" untested devices, and bypass the normal process through which investigational products are proven safe and effective, possibly exposing patients to unwarranted risks.

Once the single, allowable emergency use has occurred, we believe it is reasonable that users will be able to anticipate the vast majority of potential future uses and needs for the device, and therefore the guidance prohibits the manufacturer from shipping more devices to potential users until we have approved a clinical investigation. I should note here that we are required to act on an application for an IDE within 30 days.

A case in point is the recent implant of the smaller-sized version of the Jarvik-7 heart in a young woman in Minneapolis. As I indicated earlier, this device is not under an IDE. Its one-time emergency use did conform to the guidance, and we have notified the manufacturer that an IDE must be granted before the smaller heart may be used again, absent an extraordinary situation.

CONCLUSION

In closing, Mr. Chairman, I want to stress that the opportunities and problems surrounding the experimental use of the artificial heart dramatically illustrate the situation we face in regulating new medical technologies. Under such situations, we are required to carefully balance competing worthwhile goals in order to ensure prompt availability of new safe and effective therapies while maintaining needed safeguards for patients and research subjects. Let me emphasize, too, what often is forgotten in the excitement surrounding dramatic new technologies. That is, this is very preliminary research not unlike a Phase I drug study and its purpose is to explore essential, but preliminary, human knowledge.

The first of these goals is to bring to the patients valuable new products that can enhance and prolong life, and to do so with as little delay as possible. Examples of such breakthrough devices which recently we have approved are: (1) the magnetic resonance imaging device, which gives clinicians a "window" into the human body without surgical intervention; (2) the implantable defibrillator, which corrects life-threatening rhythm disturbances of the heart and provides instantaneous, life-saving resuscitation; (3) the cochlear implant, which aids the profoundly deaf, and (4) the lithotripter, which relieves the agonizing pain associated with kidney stones without the trauma and costs of surgery. In this aspect of our role, we act as a guardian of patient safety while still serving as a facilitator, a conduit through which new products are brought to market in a timely, orderly, and properly accountable fashion.

Our second goal is to assure that human trials of new devices are conducted only on products with demonstrated promise, that they are carried out using good science in a well-defined and limited study population, and that the rights of patients to be fully informed about the risks of participating in these trials are adequately protected. Once the clinical trials are over, we have to be convinced that the evidence does indeed indicate that the device is safe and effective before we allow it to be marketed.

There is a dynamic and very delicate balance between these two goals, in which FDA as the protector of the patient is called upon to act both as an accelerator and as a brake pedal. To reconcile them requires good judgment as well as good science. We must do the best we can to avoid holding up new technologies, while at the same time being careful not to allow patients to be used in premature or ill-advised clinical trials. In the case of the artificial heart, we imposed certain restrictions to assure the scientific integrity of the study, yet we recognized the need for some freedom on the part of the investigator to gather the kind of data needed to determine the viability of the device. We have also understood that it is not our role to intervene in medical practice -- we have not stationed ourselves in the operating room; but as needed, we have interceded at various points in the study to ensure that, if appropriate, course corrections were made.

Another general problem that the artificial heart exemplifies is that we must often make decisions of major importance based on less-than-perfect information. For example, is there something intrinsic about the Jarvik-7 heart that makes strokes highly likely?

Or can changes in patient management or minor changes in design mitigate the problem? No one really knows at this point, and so, balancing the potential benefits and risks very carefully, we will proceed, but with caution.

Mr. Chairman, this concludes my statement. I would be pleased to respond to any questions you might have.

Mr. **Volkmer**. Thank you very much, Mr. Norris.

Doctor McIntosh.

Dr. **McIntosh**. Mr. Chairman, thank you very much for inviting me to participate in today's hearing concerning the proper role of Federal review of chronic implantation of the Jarvik-7 artificial heart.

I am Dr. Charles L. McIntosh, Chairman of the Food and Drug Administration's Circulatory System Devices Advisory Panel, which recently conducted a review of the 3 years of experience using the Jarvik-7 mechanical heart.

In way of introduction, let me say that I have been employed by the National Institutes of Health as a member of the Surgery Branch of the National Heart, Lung, and Blood Institute since 1968. I have been an attending cardiac surgeon since 1970, and a senior investigator whose research has included the systematic evaluation of numerous mechanical and tissue valves.

My views in testimony today reflect solely those of my own as Chairman of the Circulatory System Devices Panel, and not those of the National Institutes of Health.

May I just say a few words about the Circulatory Systems Devices Panel.

FDA advisory panels are constituted and managed by the FDA and consist of individuals with the necessary expertise to evaluate the safety and effectiveness of devices, and who are free of institutional, investigator, or financial conflict of interest.

The Circulatory Systems Devices Advisory panel, consisting of physicians, scientists, and consumer and industry representatives, was appointed to make recommendations to the FDA Commissioner regarding the safety and efficacy of implantable cardiovascular devices.

In carrying out its charge the panel have used scientific data, including *in vitro* laboratory testing and *in vivo* animal and controlled human clinical evaluation.

The panel then meets to hear the presentations by the sponsors, principal investigators, and experts concerning the device under investigation. Questions are asked by the panel and the FDA for clarification of data to explore areas of concern or labeling for the device.

The panel then recommends to the FDA Commissioner that the device be approved with or without provisos or not be approved.

Let me now summarize the recent panel review of clinical experience with the Jarvik-7 heart to date. As I am sure you know, stroke, postoperative bleeding, anticoagulation complications, hemolysis, respiratory and renal problems have posed significant problems in these patients.

On December 20 of last year the panel convened in Washington, DC, to review the information supplied by Symbion, and the Humana research team in response to the panel's questions, and to discuss our concerns directly with them.

The basic charge to the panel was to evaluate probable causes of the complications and to attempt to decide whether they were related to clinical management or the device itself, or both, and to make recommendations to the FDA concerning the future of the Mechanical Heart Program at Humana.

In broad terms, the options included: To allow the program to continue with no major changes for the next three implants; to allow the program to continue with specified provisos to the protocol, or, to terminate the investigation because major changes in the devices were necessary.

The panel's review of the data confirm the magnitude and complexity of this investigation, as well as the important scientific information that has been gained from the four mechanical heart implants. The recipients thus far have not been transplant candidates on the basis of age and/or coexisting diabetes mellitus.

All patients were critically ill and confined to the hospital secondary to idiopathic or ischemic cardiomyopathy. All four patients were judged to be within days of death despite maximal medical therapy and intravenous drugs to maintain their blood pressure and perfusion of vital organs.

Chronic renal insufficiency and mild chronic obstructive pulmonary disease were present in all patients preoperatively which constitutes potential risk for further renal and pulmonary complications in the postoperative period.

I would like to briefly discuss the reported complications and solutions proposed by Dr. DeVries and his colleagues.

The major complication has been stroke and the critical question has been how to prevent this in patients receiving a Jarvik-7 mechanical heart. Strokes and complications associated with anticoagulation therapy are not unique to the Jarvik-7. They continue to be major problems in patients requiring either a tissue or mechanical heart valve and in other forms of cardiovascular disease.

Multiple causes of stroke include: an embolus or blood clot, originating from the device, suture lines, or from diseased arteries outside the heart; hemorrhage into the brain which may occur spontaneously in patients with hypertension or complications related to anticoagulation use or to infected materials or vegetations which travel to the brain similar to a clot.

The multiple potential causes of stroke make it difficult to implicate the device using current tests. CAT scans and cerebral arteriograms will be routinely performed preoperatively on these patients to rule out some potential sources of stroke.

Two of the four patients have had a total of five strokes. One patient has suffered four events, two embolic and two hemorrhagic, and remains neurologically impaired. The second patient has had one embolic stroke and has had a good neurologic recovery.

The mechanisms of blood clot formation are extremely complex, and the Jarvik-7 investigations use both routine and extended monitoring of these parameters and is outlined in my written testimony. Clinical information gained from the four recipients of this device and the coagulation symposium sponsored by Symbion provide the currrent rationale for optimal monitoring of patients.

As important as monitoring is the type and timing of anticoagulation therapy used to prevent clot formation and minimize bleeding complications in early and late postoperative periods.

Basically, there are four anticoagulant drugs in current clinical use: Heparin, sodium warfarin, aspirin, and dipyridamole.

The proposed anticoagulation regimen uses extended monitoring of clotting factors and combinations of anticoagulants to minimize clot and/or hemorrhagic complications. The panel felt that the neurologic complications, that is stroke, were both device- and management-related, and that the new monitoring and anticoagulation regimen may potentially decrease this risk in future patients.

All four patients required a second operation after having a Jarvik-7 implanted, three for bleeding complications and one to repair an air leak from a ruptured bleb on the lung. Postoperative bleeding from the posterior aortic suture line occurred in two patients, necessitating large transfusions of blood and blood products which may potentially affect renal and pulmonary function.

The third patient who was fully anticoagulated, bled after a monitoring line was removed and required multiple transfusions and reoperation. These bleeding complications have prompted a more aggressive approach to early reoperation to avoid large transfusions.

Altered suturing techniques and revised handling of monitoring lines may also decrease the risk of postoperative bleeding and will be added to the new protocol.

In patients with preexisting renal and respiratory insufficiency, bleeding requiring blood transfusions, as well as other factors, may further compromise the functions of these systems. All four patients developed acute tubular necrosis, or ATN, resulting in marked decrease in urine production and associated fluid, nitrogen, and potassium retention.

The ATN was self-limited in three patients, but necessitated dialysis in the fourth, which contributed to his death. The breakdown of blood cells following massive transfusions, or the destruction of blood cells due to the heart-lung machine, the Jarvik-7, or its drive system, may overwhelm the filtering capacity of the kidneys, causing further insufficiency.

The revised protocol will include the use of drugs intra-and postoperatively to enhance renal function, optimization of drive system dynamics, and avoidance, when possible, of large transfusions.

Respiratory function may be adversely affected by volume overload associated with ATN or by the deposition in the lung of the breakdown products from blood cells.

Again, the panel felt that respiratory insufficiency could be minimized in future patients by decreasing the direct and indirect effect of large transfusions on the lungs.

Hemolysis, the breakdown of the red blood cells, may be caused by turbulent blood flow through a device such as the heart-lung machine, artificial heart valves, or the Jarvik-7 heart and its drive system, or be secondary to transfusion or drug reaction. The two surviving patients continue to require periodic blood transfusions to maintain their hemoglobin level in an acceptable range.

Specific changes in the operation of the Utah drive system have decreased the rate of hemolysis and may decrease the need for tranfused blood in current and future recipients.

Patients receiving the Jarvik-7 heart are subject to the usual infections observed in other cardiac surgical patients, that is pneumonia, urinary tract infections, blood infections, or infection of the device itself. These patients are unique in that they are tethered to the external drive system by lines which enter their chest cavity via skin buttons.

These skin buttons are potential sites of infection which originate on the skin and may penetrate along the lines to the mechanical heart and chest cavity.

The new protocol will require complete isolation technique in the care of these exit sites including, gloves, masks, and gown precautions when areas are inspected or dressings changed. Body CAT scans will also be utilized to detect potential hidden infections along these lines.

This concludes the major complications and their causes as well as possible solutions presented to the panel. The panel's recommendation to continue the protocol was supported by the accumulation of valuable scientific data some of which are unique to this investigation. These data include hemodynamic changes, observed in response to implantation of the total artificial heart; altered cardiovascular dynamics; pharmacological response to various cardiovascular drugs; exercise performance and associated hemodynamic changes, beneficial or adverse effects on other organ systems; long-term effects on blood cell components and coagulation factors; chronic monitoring of these patients; and long-term durability of the Jarvik-7 and the Utah-drive system.

The panel was assured that data management includes accurate collection, storage, and analysis, and that scientific articles will be submitted in peer reviewed journals in the near future.

New areas of interest that have been stimulated by the current investigations include: The nutritional status of these debilitated patients and methods for supporting acute and chronic metabolic needs; absorption patterns of drugs; extended monitoring of coagulation profile for optimal anticoagulation therapy, and immunological responses observed in these individuals.

Based on the scientific data reviewed and presented to the panel, the following recommendations were submitted to the FDA Commissioner. The panel unanimously voted that the total artificial heart project at Humana be continued, contingent upon the following conditions.

One, the FDA is to assume a more direct oversight role as the clinical trial proceeds and should approve subsequent plans on a case-by-case basis. That is, data derived from each succeeding implant must be submitted to the FDA for review on a quarterly basis as a condition for future implants.

Two, the sponsor should submit to, and have approved by the FDA, a revised investigational device exemption or IDE protocol, that specifies the steps to be taken in clinical patient care and data acquisition. The revised protocol should delineate those changes to be made in patient management and identify additional collaborators who can bring expertise in the fields of immunology, hematology, nephrology, biostatistics and other disciplines as needed.

And three, the FDA should consult with the panel in carrying out these provisions.

Mr. Chairman, this concludes my statement. I would be pleased to respond to any questions you or members of your committee may have.

[The prepared statement of Mr. McIntosh follows:]

STATEMENT

BY

CHARLES L. MCINTOSH, M.D., PH.D.

CHAIRMAN

CIRCULATORY SYSTEM DEVICES ADVISORY PANEL

U.S. FOOD AND DRUG ADMINISTRATION

BEFORE THE

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

FEBRUARY 5, 1986

Mr. Chairman and Members of the Subcommittee:

Thank you very much for inviting me to participate in today's hearing concerning the proper role of Federal review of the chronic implantation of the Jarvik-7 artificial heart. I am Dr. Charles L. McIntosh, Chairman of the Food and Drug Administration's Circulatory System Devices Advisory Panel, which recently conducted a review of the three years of experience using the mechanical heart designed by Symbion, Inc., and implanted in four patients by Dr. William DeVries.

By way of introduction, let me say that I am employed by the National Institutes of Health as a member of the Surgery Branch of the National Heart, Lung, and Blood Institute since 1968. I have been an attending cardiac surgeon since 1970 and a senior investigator whose research has included the systematic evaluation of numerous mechanical and tissue heart valves and clinical evaluation and implantation of the first atomic powered pacemaker. My testimony today solely reflects my own views as Chairman of the Circulatory System Devices Panel, and not those of the NIH.

My association with the Panel began in 1980, when I joined as a voting member. I served in that capacity for four years and then remained as a consultant to the Panel. I accepted my current appointment as Panel Chairman in 1985.

ROLE OF THE CIRCULATORY SYSTEM DEVICES PANEL

FDA advisory panels are constituted and managed by FDA and consist of individuals with the necessary expertise to evaluate the safety and effectiveness of devices, and who are free of institutional, investigator, or financial conflict-of-interest.

The Circulatory System Devices Advisory Panel, consisting of physicians, scientists, and consumer and industry representatives, is appointed to make recommendations to the FDA Commissioner regarding the safety and efficacy of implantable cardiovascular devices. Devices reviewed by the Panel have included heart valves, pacemakers, oxygenators used in heart-lung machines, vascular grafts, diagnostic and therapeutic catheters, implantable defibrillators, and the subject of today's hearing, the Jarvik-7 mechanical heart. In carrying out its charge, the Panel reviews scientific data including in vitro laboratory testing and in vivo animal and controlled human clinical evaluations.

Evaluations of a device must be based upon past performances of other regulated devices as in the case of heart valves, pacemakers, etc. In the case of the Jarvik-7 mechanical heart, there was no precedent to rely on.

RELATIONSHIP BETWEEN IRBs, FDA, AND THE PANEL

I would like to briefly comment on the respective roles of local Institutional Review Boards (IRBs), the FDA, and the Panel in overseeing and regulating clinical device investigations such as the implantation of the Jarvik-7 mechanical heart.

The local IRB is the "watchdog" of the institution in which a clinical study is being conducted. In this capacity, it is responsible for evaluating the scientific merit and methodology of the investigation; the benefits and risks to patients; bioethical issues; and the environmental impact the study will have on institutional personnel, costs, and services. Typically, IRBs are comprised of clinicians, basic scientists, administrators, a bioethicist, and either a clergyman or lay person from the local community. Most clinical investigations generally relate to drugs, radiation, genetic engineering, or operative treatment of diseases. Very few focus on a device such as the Jarvik-7 heart as the primary therapeutic modality. Depending upon the institution and the device, IRBs may or may not possess the requisite expertise to evaluate the product in question.

The Division of Cardiovascular Devices in the FDA's Center for Devices and Radiological Health functions as interpreter of the law, organizer, preliminary reviewer, and liaison between the sponsor/investigator and the Panel, and the regulator of devices. The FDA is a valuable resource to the Panel for it is the "keeper of the archives" containing past performance, results, complications, and post-marketing surveillance information about devices produced since the Medical Device Amendments of 1976. Once the laboratory and clinical trials are completed by the sponsors/investigators and reviewed by FDA, the scientific data are sent to the Advisory Panel for its review prior to the formal meeting.

The Panel then meets to hear presentations by the sponsors, principal investigators, and experts concerning the investigation of the device. Questions are then asked by the Panel and FDA for clarification of data to explore areas of concern or the labeling for the device. The Panel then recommends to the FDA Commissioner that the device be approved with or without provisos or not be approved.

PANEL REVIEW OF THE JARVIK-7 HEART

Let me now summarize the events leading up to the recent Panel review of the clinical experience with the Jarvik-7 heart to date. FDA regulations require that periodic and yearly reports on the progress of clinical investigations be made to appropriate IRBs, and for significant risk devices like the artificial heart, sponsors must submit such reports to FDA. In compliance with these requirements, officials of Symbion, Inc., the manufacturer of the Jarvik-7 heart, requested Dr. DeVries, the principal investigator, to submit his data on the first four implant recipients for review. Members and consultants of the Panel examined this material and felt that a Panel meeting would be the appropriate forum to evaluate problematic areas and possible solutions. As I am sure you know, strokes, post-operative bleeding, anti-coagulation complications, and respiratory and renal problems have posed significant problems in these patients.

The complexity of review of the clinical results of the four implanted Jarvik-7 hearts, and the short time period within which this was to be accomplished, necessitated several changes in the Panel and in the manner that the Panel review would be conducted. Several areas of expertise were necessary to review this device which were not present on the Panel as originally constituted, and therefore four additional consultants from other FDA panels were asked to participate. Specifically, specialists in hematology, immunology, neurology, and biomaterials participated in this latest review.

Normally, one member of the Panel serves as the primary reviewer of a given device, but since the mechanical heart crossed so many disciplines, each Panel member was asked to function as a reviewer in his specialized field. Additional data were requested from Symbion concerning transcripts from a three-day workshop concerning the problem of strokes and anti-coagulation in patients receiving a mechanical heart implant. These data were also shared with appropriate Panel members for review.

There were many questions to be answered in a brief time period and therefore each Panel member and consultant was requested to submit his specific questions in writing to the FDA. These questions were compiled into problem areas and then forwarded to Drs. Jarvik and

DeVries for the purpose of aiding their discussion and preparation for the formal Panel meeting. This also permitted the company and Humana officials to assemble appropriate consultants to participate in the meeting to facilitate discussion on the wide range of specific issues.

PANEL MEETING

On December 20 of last year, the Panel convened in Washington, D.C. to review the information supplied by Symbion and the Humana research team in response to the Panel's questions, and to discuss our concerns directly with them. The basic charge to the Panel was to evaluate probable causes of the complications I have discussed previously, and to attempt to decide whether they were related to clinical management, the device itself, or both, as well as to make recommendations to FDA concerning the future of the mechanical heart program at Humana. In broad terms, the options included: to allow the program to continue with no major changes for the next three implants; to allow the program to continue with specified provisos to the protocol; or, to terminate the investigation because major changes in the device were necessary.

The Panel meeting was conducted in three stages: a public forum, at which members of the public-at-large addressed the Panel; a closed session, at which Symbion officials and Dr. DeVries and his associates discussed the experiences of the first four implant recipients; and an executive session, at which the Panel held private deliberations about the future course of the Jarvik-7 investigation. Mr. Chairman, I have attached to my testimony a list of the Panel members and consultants who participated in this review.

The witnesses who appeared at the public session, many of whom are participating in today's hearing, and their statements are a matter of public record, and so I will not try here to characterize the public portion of the meeting. During the closed session, the Panel received and reviewed proprietary and confidential patient information. The data focused on the pre-operative assessment of each of the four patients, including primary cardiovascular diagnosis, current functional class, and previous medical regimens, clinical evaluation of renal, respiratory and hemodynamic status, laboratory evaluations, and the reasons patients were not considered as transplant candidates. Operative notes for initial implantation and subsequent operations for persistent bleeding, as well as the associated anti-coagulation regimen for each patient, were also reviewed. I have also attached to my testimony an outline of the data the Panel requested from Symbion and Dr. DeVries.

BASIS OF THE PANEL'S RECOMMENDATIONS

Background:

The Panel's review of the data confirmed the magnitude and complexity of this investigation, as well as the important scientific information which has been gained from the four mechanical heart implants. Only two percent of patients thus far screened as implant recipients have been accepted or have elected to receive the Jarvik-7. All recipients thus far have not been transplant candidates on the basis of age (61, 54, 58, and 62 years), or co-existing diabetes mellitus. (Most transplant centers set 50 years of age as the upper limit. This has recently been increased to 55 years.) Review of medical records revealed that all patients were critically ill and confined to the hospital (functional Class IV as defined by the New York Heart Association), secondary to idiopathic or ischemic cardiomyopathy. All four patients were judged to be within days of death despite maximal medical therapy and intravenous drugs to maintain their blood pressure and perfusion of vital organs. Chronic renal insufficiency and mild chronic obstructive pulmonary disease were present in all patients pre-operatively which constitutes potential risk for further renal and pulmonary complications in the post-operative period. Prior to implantation, patients and their families received approximately 100 hours of information and counseling before consenting to the operation.

At the time of the Panel meeting, two patients continued to live with a total mechanical heart (380 and 296 days respectively following implant). Death in the first patient at 112 days was due to complications related to long-term antibiotic administration and bleeding complication following dialysis 10 days post-operatively in the fourth.

As I mentioned previously, the Panel's charge was to review the safety and efficacy of the Jarvik-7 mechanical heart and to decide whether reported complications were solely device-related, clinical management-related, or a combination of the two. Because much of the information concerning the Jarvik-7 heart presented to the Panel involves proprietary data or patient confidentiality, I cannot discuss specific details of each patient's clinical course. I can provide a general overview of the relevant scientific data submitted and proposed solutions which support the Panel's recommendations.

COMPLICATIONS AND PROPOSED SOLUTIONS

Stroke, Anti-Coagulation and Therapy:

The major complication has been "stroke" and the critical question has been how to prevent this in patients receiving a Jarvik-7 mechanical heart. Strokes and complications associated with anti-coagulation therapy are not unique to the Jarvik-7, for they continue to be major problems in patients requiring either a tissue or mechanical heart valve and in other forms of cardiovascular disease.

Multiple causes of "stroke" include: an embolus (blood clot) originating from the device, suture lines or from diseased arteries outside the heart, hemorrhage into the brain which may occur spontaneously in patients with hypertension or complications related to the use of anticoagulants, or infected material or "vegetations" which travel to the brain similar to a clot. The multiple potential causes of "stroke" make it difficult to implicate the device using current tests. CAT scans and cerebral arteriograms are now routinely performed pre-operatively on these patients to rule out some potential sources of stroke.

Two of these four patients have had a total of five "strokes." One patient has suffered four events, two embolic and two hemorrhagic, and remains neurologically impaired. The second patient has had one embolic stroke and has had good neurologic recovery.

The mechanisms of blood clot formation (hemostasis) are extremely complex, and various types of emboli may occur. Routine monitoring of hemostasis has included tests such as platelet count, prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen levels, and bleeding time. More recently, extended monitoring includes fibrinopeptide A (assays in vivo thrombin activity), platelet Factor IV, beta thromboglobulin (estimates in vivo platelet aggregation) and an assay for thromboxane B-2. I list these laboratory tests not to confuse the issue, but rather to emphasize the complexity of monitoring blood clotting factors which may indicate inappropriate anti-coagulation or a potential set-up for a stroke. Currently, the two surviving patients have the above tests performed weekly, as will future patients. Clinical information gained from the four recipients of the Jarvik-7 heart and from the coagulation symposium sponsored by Symbion provide the current rationale for optimal monitoring of patients.

As important as monitoring is the type and timing of anti-coagulation therapy used to prevent clot formation and minimize bleeding complications in the early and late post-operative periods. Basically, there are four anti-coagulant drugs in current clinical use: heparin, sodium warfarin (Coumadin), aspirin, and dipyridamole (Persantine). Heparin and sodium warfarin inhibit key steps in the clotting mechanism so that fibrin clots will not be produced. Heparin is administered intravenously or under the skin and is relatively short acting. Sodium warfarin is taken orally and may take 3-4 days to disappear from the blood once stopped, unless reversed by other agents. Aspirin and dipyridamole act to prevent the aggregation of platelets, which initiates the clotting mechanism. Aspirin has been associated with increased risk of bleeding and therefore its use in these patients is reserved for special indications.

The proposed anti-coagulation regimen uses extended monitoring of clotting factors and combinations of anti-coagulants to minimize clot and/or hemorrhagic complications. The Panel felt that the neurologic complications (i.e., stroke) were both device and management-related, and that the new monitoring and anti-coagulation regimen may potentially decrease this risk in future patients.

Reoperation in Patients Implanted With the Jarvik-7:

All four patients required a second operation after having a Jarvik-7 implanted, three for bleeding complications and one to repair an air leak from a ruptured bleb on the lung. Post-operative bleeding from the posterior aortic suture line occurred in two patients, necessitating large transfusions of blood and blood products which may potentially effect renal and pulmonary function. It was hoped that the bleeding would stop once the coagulation profile was optimized and that a repeat operation with its potential complications would be avoided. One of these patients also had diffuse bleeding from the sternum, which had to be removed to permit placement of the Jarvik-7. This problem may be avoided by pre-operative chest CAT scan to evaluate chest cavity configuration and size. The third patient, who was fully anti-coagulated, bled after a monitoring line was removed and required multiple transfusions and reoperation. These bleeding complications have prompted a more aggressive approach to early reoperation to avoid large transfusions. Altered suturing techniques for posterior aorta line and revised handling of monitoring lines may also decrease the risk of post-operative bleeding and will be added to the new protocol.

Renal and Respiratory Complications:

In patients with pre-existing renal and respiratory insufficiency, bleeding requiring blood transfusions as well as other factors may further compromise the functions of these systems. All four patients developed acute tubular necrosis (ATN), resulting in marked decrease in urine production and associated fluid, nitrogen, and potassium retention. The ATN was self-limited in three patients, but necessitated dialysis in the fourth, which contributed to his death. The breakdown products of blood cells following massive transfusions, or the destruction of blood cells (hemolysis) due to the heart-lung machine, the Jarvik-7, or its drive system, may overwhelm the filtering capacity of the kidneys, causing further insufficiency. The revised protocol will include the use of drugs intra- and post-operatively to enhance renal function, optimization of drive system dynamics, and avoidance, when possible, of large transfusions.

Respiratory function may be adversely affected by volume overload associated with ATN or by the deposition in the lungs of breakdown products from blood cells. Post-operative bleeding or infection may result in dense scar tissue entrapping the lung, which can decrease respiratory function, prolonging the need for ventilatory support. This may be a significant factor in one surviving patient who continues to require intermittent ventilator support. Again, the Panel felt that respiratory insufficiency could be minimized in future patients by decreasing the direct and indirect effect on the lungs of large transfusions.

Hemolysis:

Hemolysis may be caused by turbulent blood flow through a device such as the heart-lung machine, an artificial heart valve, or the Jarvik-7 heart and its drive system, or be secondary to a transfusion or drug reaction. The two surviving patients continue to require periodic blood transfusions to maintain their hemoglobin level in an acceptable range. The Hall-Kaster valves now being used in the Jarvik-7 are known to produce slight hemolysis, but they are extremely durable devices and will continue to be used in future Jarvik-7 mechanical hearts. Specific changes in the operation of the Utah drive system have decreased the rate of hemolysis and may decrease the need for transfused blood in current and future recipients.

Infections:

Patients receiving the Jarvik-7 heart are subject to the usual infections observed in other cardiac surgical patients, i.e., pneumonia, urinary tract infections, blood infections (sepsis), or infection of the device itself. These patients are unique in that they are tethered to the external drive system by lines which enter their chest cavity via "skin buttons." These "skin buttons" are potential sites of infection which originate on the skin and penetrate along the lines to the mechanical heart and chest cavity. One patient has a chronic infection of this site, but no evidence of a deep-seated infection. The new protocol will require complete isolation technique in the case of these exit sites including, gloves, masks, and gown precautions when areas are inspected or dressings changed. Body CAT scans will also be utilized to detect potential hidden infections along these lines.

Continued Scientific Data Resource:

The Panel's recommendation to continue the protocol was also supported by the accumulation of valuable scientific data, some of which is unique to this investigation. These data include hemodynamic changes observed in response to implantation of the total artificial heart, altered cardiovascular dynamics, pharmacological response to various cardiovascular drugs, exercise performance and associated hemodynamic changes, beneficial or adverse effects on other organ systems, long-term effects on blood cell components and coagulation factors, chronic monitoring of these patients, and long-term durability of the Jarvik-7 and the Utah drive system. The Panel was assured that data management includes accurate collection, storage, and analysis, and that scientific articles will be published in peer review journals in the near future.

New areas of interest that have been stimulated by the current investigations include: the nutritional status of these debilitated patients and methods for supporting acute and chronic metabolic needs; absorption patterns of drugs; extended monitoring of coagulation profile for optimal anti-coagulation therapy; and immunological responses observed in these individuals. Immunologic studies may delineate the humoral and cellular response of the immune system to a chronically implanted artificial heart and may be of diagnostic or therapeutic importance in future investigations of this product.

PANEL'S RECOMMENDATIONS

Based on the scientific data reviewed and presented to the Panel, the following recommendations were submitted to the FDA Commissioner. The Panel unanimously voted that the total artificial heart project at Humana be continued, contingent upon the following conditions:

1. The FDA is to assume a more direct oversight role as the clinical trial proceeds and should approve subsequent plans on a case-by-case basis. That is, data derived from each succeeding implant must be submitted to the FDA for review on a quarterly basis as a condition for future implants.

2. The sponsor should submit to, and have approved by FDA, a revised Investigational Device Exemption (IDE) protocol that specifies the steps to be taken in clinical patient care and data acquisition. The revised protocol should delineate those changes to be made in patient management and identify additional collaborators who can bring specialized expertise in the fields of immunology, hematology, nephrology, biostatistics and other disciplines as needed.

3. The FDA should consult with the Panel in carrying out these provisions.

Mr. Chairman, this concludes my statement. I would be pleased to respond to any questions you or members of the Subcommittee might have.

Mr. **Volkmer**. Thank you very much, Mr. McIntosh—Dr. McIntosh, for your statement.

Before I begin with my questions, I would like to ask Mr. Norris if he has anything. He had a 3:30 appointment elsewhere. Where is that so I can give you——

Mr. **Norris**. That is over at Health and Human Services.

Mr. **Volkmer**. It was in this building then?

Mr. **Norris**. No, no; it is a 15-minute walk from here.

Mr. **Volkmer**. You are not talking about the subcommittee; I thought you were talking about that——

Mr. **Norris**. No, no, I am sorry.

Mr. **Volkmer** [continuing]. The Waxman subcommittee.

You are down a——

Mr. **Norris**. I have got a press conference, that is scheduled for 3:30.

Mr. **Volkmer**. All right, I am going to try and do you—I have a quick question, if we can——

Mr. **Norris**. Well, Dr. Mohan can answer if I have to leave before you are completed. Dr. Mohan can answer——

Mr. **Volkmer**. Submittal in writing, all right?

[See written questions, p. 345.]

I would like to just go over, when you were mentioning the bridge——

Mr. **Norris**. Bridge-to-transplant.

Mr. **Volkmer** [continuing]. Implants that had taken place in the last few days, we have information that on, I believe, it was Monday, Dr. Griffith, also implanted a Jarvik-7, and that he has approval to do this and also that he has approval to do a total of 10, is that correct?

Mr. **Norris**. Your information is correct. I think that was in an earlier chart.

Mr. **Volkmer**. That's all right. I just want to make sure we get that. And also now Dr. Copeland has also permission to a bridge—10 bridges with the Jarvik-7, is that——

Mr. **Norris**. That is correct.

Mr. **Volkmer**. And Dr. Joyce?

Mr. **Norris**. Also has 10. These are the Jarvik-7 100 cc hearts.

Mr. **Volkmer**. That is the larger one. And Dr. Pierce?

Mr. **Norris**. And Dr. Pierce, yes, at Hershey, that is correct.

Mr. **Volkmer**. Are there any others?

Mr. **Norris**. Let me just clear up on that.

Dr. Pierce's are the Penn State heart, not the Jarvik-7.

Mr. **Volkmer**. All right, the Penn State for Dr. Pierce?

Mr. **Norris**. That is right.

Mr. **Volkmer**. All right now, are there any other physicians approved for the use of any other artificial device for bridging purposes?

Mr. **Norris**. Yes, Dr. Cooley was approved for an emergency device implantation.

Mr. **Volkmer**. All right, that was after the fact though, mostly, was it not?

Mr. **Norris**. No, no, it was long in advance of the fact. We gave him our consent several months ago, in May 1985, we gave him consent to—advance consent to implant one bridge-to-transplant for the 100 cc Jarvik-7 heart.

Mr. **Volkmer**. Have they improved the informed consent deficiencies?

Mr. **Norris**. Let me ask Dr. Mohan if he will respond to that.

Dr. **Mohan**. Yes, Mr. Chairman, I guess what you are referring to is the fact that to be conditionally approved, Dr. Cooley. We had, I believe, some problems with including him as another center in the bridge study, but we said that, while certain deficiences are being corrected, if there is an emergency, you can use this heart. There were some deficiencies, I believe, if my memory is correct, which were to be corrected. Some of them were, I don't remember exactly if all of them were or not. And again, I am speaking from memory here, but we never retracted the original permission that we had given him.

So the bottom line as far as our records so far seem to indicate is that the permission that we had granted him for an emergency holds.

Mr. **Volkmer**. All right. So, it is contemplated that we will be seeing in the near future additional emergency type of bridge implants. Is that correct?

Mr. **Norris**. As appropriate, there is a maximum number of implants permitted, as you indicated earlier, 10——

Mr. **Volkmer**. I know—within that number?

Mr. **Norris**. Yes.

Mr. **Volkmer**. So we are anticipating we are going to see some?

Mr. **Norris**. We are anticipating that, yes.

Mr. **Volkmer**. As we progress with these, where does the feedback go back to, as to the data on the conditions, similar to what Dr. DeVries has to do? In other words, how are we going to learn from this and the use of it? Who are they going to report it all back to, as to conditions of patients, et cetera, whether it was blood clotting, all this, because they are going to be able to take those hearts back out again, are they not?

The artificial ones; it is contemplated they are going to, and you're going to have a transplant, so——

Dr. **Mohan**. Yes, sir. In the requirements of the proposed emergency guidelines, which are proposed at this time, that we have, under which people are operating, we do require that once an emergency implant is done, the results of that be reported back to FDA. And also, if it is on a device which is already part of another IDE, the report has to go back to the sponsor of that device, and then through the normal reporting mechanisms, that information gets built in.

If I may add, when we were talking about the 70 cc heart, for example, we already received some of the information on the Minneapolis implant. That information was taken into consideration when we made the decision to allow an emergency implant of the 70 cc heart by Dr. Copeland in Tucson.

Mr. **Volkmer**. Is that the only 70 cc that has been implanted?

Mr. **Norris**. No, it is not; no.

Mr. **Volkmer**. Well, who else used it?

Mr. **Norris**. On this chart right before you there, the 70 cc has been implanted by Dr. Joyce at Abbott-Northwestern Hospital. In

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addition, as I stated in my testimony at the University of Arizona, Dr. Copeland, just a couple of days ago——

Mr. VOLKMER. All right, the one a few days ago, was a 70 cc?

Mr. NORRIS. That is correct.

Mr. VOLKMER. OK. Now therefore, this approval to Dr. Copeland is for both the 100 and the 70 cc?

He can use either one interchangeably?

Dr. MOHAN. Yes, sir. The approval to Dr. Copeland for the 100 cc heart is for 10 patients all together. And he has permission to do that.

In addition, as part of the emergency provisions he asked us for this one case, and he was given permission for this one additional implantation. He does not at this time have permission for additional implantations of the 70 cc heart.

Mr. VOLKMER. I am glad you cleared that.

That would apply also then to Dr. Joyce in Minnesota, is that correct?

Dr. MOHAN. Yes, sir.

Mr. NORRIS. That is correct. Our expectation——

Mr. VOLKMER. So, if anybody wants to use the 70 cc, they are going to have to come to you to get the consent before they can use it?

Mr. NORRIS. Until the device is under an IDE, which we are expecting it to be shortly.

Mr. VOLKMER. All right. OK.

Now how do you regulate the left ventricle assist devices?

How does it compare to the regulation of the artificial hearts?

Dr. MOHAN. There are again, a number of left ventricular assist devices which are in the investigation stage. And they are regulated like the artificial heart is regulated, the same kinds of rules, reporting mechanisms, et cetera.

Mr. VOLKMER. OK. Where are the results obtained on the LVAD's reported?

And are they made public; or could they be made public?

Is there proprietary information there? I am just——

Dr. MOHAN. So far as all investigational device exemption studies are concerned, we get annual reports on the results, and all these LVAD's. The results are being reported to us on an annual basis, unless there is a particular problem with one, and we can ask for more frequent reports.

We do not, and cannot by law, make that sort of data public and cannot publish it. That is for the investigator to do, and we certainly encourage it.

Mr. VOLKMER. All right. Now to get back to the approval on the use of the artificial heart on a "type emergency basis," does that mean we really don't have a guideline, that as long as the doctor considers it an emergency, that he can go ahead and use it?

Mr. NORRIS. We have a guidance, it is a proposed guidance. Our hope is that through our support of manufacturers that they will submit IDE's on a timely basis to us. So that we are not "hanging out there" for even one-time uses outside of an IDE.

What we attempted——

Mr. VOLKMER. Yes, but it is happening?

Mr. **Norris**. It's happening. What we have attempted to craft is a methodology that allows us not to involve ourselves in second guessing physicians who are caught in emergency situations.

Rather, we would prefer to deal with manufacturers in supporting them in getting the information to us on a timely basis.

As indicated earlier, we are required by statute to respond to the manufacturer once he has a submission to us within 30 days. So, we can act very, very timely on this if we get the information from the manufacturer.

Mr. **Volkmer**. Oh, I had one—I would like to, because I have got a vote on, too.

Mr. **Norris**. All right.

Mr. **Volkmer**. We are going to recess in just a few minutes. At that time you will be able to leave.

Do we have any idea when the FDA will respond to Symbion's and Dr. DeVries' supplement to the IDE, in other words, to continue their research?

Mr. **Norris**. We will respond on a very timely basis. We have a meeting scheduled immediately after this hearing with Symbion to discuss, among other things, their supplemental submission of a complete IDE package for the Jarvik 70 cc heart.

We are hopeful that our support of their activities results in these being completely, these loose issues being completely cleaned up within 30 days of today.

Mr. **Volkmer**. In other words, we're looking at, hopefully, no longer than a 30-day deadline?

Mr. **Norris**. That's correct.

Dr. **Mohan**. Actually, if I may, I would add, Mr. Chairman, that 30 days really starts from the time we receive the application. We will respond within 30 days, as we are required to do by law, and as we do on a regular basis with all IDE applications, within 30 days of receipt.

Mr. **Volkmer**. Now, there have been some people that have been concerned that, until the December 20 meeting of FDA Circulatory System Device Advisory Panel, there had been little review of the data obtained on the Jarvik-7, the 100 cc, and the clinical trial. How do you respond to those concerns?

Dr. **Mohan**. We had, as was pointed out, Mr. Chairman, in Mr. Norris' testimony, we had a few occasions to intercede in this study. When we got—we started receiving some reports of the strokes and the continuing problems, some of it through the popular literature, because the expectations regarding the publication of this data in refereed journals wasn't really being met, because the investigator was busy with other things, and so on. So because there was a paucity of data when we started receiving the reports of these complications, we got concerned. We asked the sponsor for a report on the status of the results of the first four patients. We got that. We had some concerns, and our panel had some concerns with what was reported to us. And it was thought necessary to go in and do some more detail. And that is why the panel meeting was organized.

If I may add, on a very rapid scale—within a matter of a couple or 3 weeks—we were able to get together people from all over the country to come and give a thorough scientific scrutiny of this data and to come out with the recommendations that the panel did come out with.

Mr. VOLKMER. Mr. Norris, is Dr. DeVries the only physician who has applied to do permanent implants?

Mr. NORRIS. That's correct, Mr. Chairman.

Mr. VOLKMER. And with the number of temporary or mercy type of implants that will be occurring because of the numbers that have been approved, do you contemplate that some of those may become permanent?

Mr. NORRIS. I think there's a real risk that we will have some temporary bridge-to-transplant that will become *de facto* permanent transplants. I think——

Mr. VOLKMER. What do we do in that instance?

Mr. NORRIS. Pardon?

Mr. VOLKMER. What do we do in that instance?

Mr. NORRIS. Well, I think——

Mr. VOLKMER. Do those patients and the physicians then come under the same protocol, and so forth, that Dr. DeVries is under?

Mr. NORRIS. Well, first of all, we are requiring the institutions that are doing bridge-to-transplants to also satisfy protocols that they would be willing and able to handle a situation that could arise that the patient would become, de facto, a permanent recipient. Now, I am assuming no ill will is involved in the transaction, according to your description. It simply turns out that the patient is never——

Mr. VOLKMER. Or something occurs: You could have a stroke; you could have kidney failure; you could have these things while you're still waiting for the transplant. And then the candidate is no longer a candidate for a transplant.

Mr. NORRIS. I understand——

Mr. VOLKMER. You're trying to hold the life through the artificial heart, maybe try and get him to recover.

Mr. NORRIS. That's a real risk. So, we have anticipated that by requiring institutions that have been approved for the bridge-to-transplants to be able and willing to take care of a patient who turns out to, de facto, become a permanent heart recipient, artificial heart recipient.

Mr. VOLKMER. What other devices do we presently have or that are being tested that would be as useful as the—for temporary; for bridging; to maintain a life until a human heart can be found? We know of the Penn State heart, the Jarvik-7 heart, and the mini-Jarvik-7. What else do we have?

Dr. MOHAN. Mr. Chairman, there are these left ventricular assist devices. But again, I would like to emphasize that all these devices are investigational, and it is a little premature for us to come to a judgment that one is better than the other. I mean, one may be very good for a particular situation; the other may be very good for a particular situation.

Mr. VOLKMER. Do we have any left ventricular assist devices that have been approved for that purpose——

Dr. MOHAN. As a bridge?

Mr. VOLKMER. As a bridge.

Dr. MOHAN. Yes.

Mr. VOLKMER. But not as experimental any longer?

Dr. **Mohan**. Approved as an investigational device, not——

Mr. **Volkmer**. That's what I mean.

Dr. **Mohan** [continuing]. Not approved for marketing.

Mr. **Volkmer**. Not approved for market. We don't have any approved for market? That's what I meant.

Dr. **Mohan**. No, no.

Mr. **Volkmer**. All right.

Does anyone, Dr. McIntosh or Dr. Lenfant, want to comment on that last statement before, as to the LVAD's, all of them being experimental, none could be better than the other, at this time?

Dr. **Lenfant**. Two of the models which are here have been approved for clinical testing, these two here.

And you also asked if some were in a development phase. These two are in a development phase.

Mr. **Volkmer**. All right.

At this time I am going to recess. Mr. Norris, if we have any additional questions, I think we should direct them solely to you. We will submit them in writing, all right? If not, we will continue when we return.

Mr. **Norris**. Good. Thank you, Mr. Chairman.

[The information follows:]

ADDITIONAL QUESTIONS AND ANSWERS FOR THE RECORD

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April 7, 1986

Mr. John Norris, Deputy Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Mr. Norris:

Enclosed is a copy of the transcript from the February 5, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight about artificial hearts. Attached to the transcript are instructions for submitting requests for changes or clarifications. Please review these instructions and the enclosed transcript of your remarks carefully.

The Subcommittee would also appreciate your written responses to the following questions:

1. Does FDA believe that the total artificial heart is a potentially useful medical product and what does the Agency see as the future of the total artificial heart?
2. Under what circumstances would FDA deny use of the artificial heart if no alternative therapy exists for a patient facing imminent death?
3. Does FDA support the development of a uniform master implant protocol so that useful, consistent scientific information could be obtained from all the centers using a particular device?
4. How many patients have had heart assist devices inserted? How many of these patients have died before a donor heart became available?
5. Has FDA reviewed Symbion's submission following the panel meeting on December 20, 1985? If so, what are the results of that review?
6. Has FDA approved the use of the Jarvik-70 cc under an Investigational Device Exemption (IDE) yet?
7. Why did FDA decide to conduct case-by-case reviews of the next three permanent artificial heart implants?

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8. Given that some temporary implants may become permanent how can FDA ensure that temporary implant patients receive the same protections and rights as patients receiving permanent implants?

9. How does FDA guarantee that the hospital in which a temporary implant has been performed is prepared to handle the possibility of the implant becoming permanent?

10. How did FDA decide to allow only one emergency use of the artificial heart while an application for an IDE is pending?

Your copy of the transcript, together with any written requests for changes, and your responses to the above questions should be returned by April 24, 1986 to:

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex I
Washington, DC 20515-6307

Your testimony at the hearing was extremely valuable to the Members, and I want to extend our thanks for your participation and service to the Subcommittee.

Sincerely,

Harold L. Volkmer
Chairman
Subcommittee on Investigations
and Oversight

HLV/Gmbh

Responses to Congressman Volkmer on Jarvik-7 Artificial Heart

Question 1: Does FDA believe that the total artificial heart is a potentially useful medical product and what does the Agency'see as the future of the total artificial heart?

Response
Part of the mission of the Food and Drug Administration is to ensure the safety and effectiveness of medical devices presented for approval by manufacturers or other sponsors. In carrying out this task, the Agency closely reviews devices like the artificial heart to assess their potential clinical value and to determine whether the benefits to the patient and to society outweigh the risks. FDA believes the artificial heart has potential clinical value and so approved it for human clinical testing. Our role is not in gauging the potential marketability or ultimate impact of a particular technology.

However, speaking as an interested bystander, the Agency believes that, when perfected, the artificial heart may be a potentially useful medical device to treat intractable heart failure and for use as a temporary bridge-to-transplant while patients await the availability of human donor hearts. Evolution of artificial heart technology could involve the development of totally implantable power sources to replace the present external drive systems. Improvements in biomaterials, valves and conduit designs will be needed, however, to reduce the high rate of thrombus formation and blood damage that is currently seen.

Question 2: Under what circumstances would FDA deny use of the artificial heart if no alternative therapy exists for a patient facing death?

and

Question 10: How did FDA decide to allow only one emergency use of the artificial heart while an application for an IDE is pending?

Response: Under FDA's proposed emergency use guidelines, the Agency would deny the use of an artificial heart if an investigational device exemption had been filed for that particular product, and after review by Agency staff, found to be so seriously deficient in concept, design, and potential medical benefit as to warrant disapproval of the IDE.

In permitting emergency use of a device that does not have an approved IDE, FDA was attempting to balance the need for control in preventing abuse by repeated "emergency" use of such a device with the need for flexibility to ensure humane treatment in responding to bona fide emergencies. Only one emergency use is allowed because we presume that a device requested for emergency use is almost ready for an IDE application. Consequently, FDA can reasonably expect to receive an IDE application before a second emergency arises.

The "one emergency use" rule is not absolute. In exceptional and well-justified cases, FDA has allowed additional emergency uses before an IDE was approved; this was the case with the 70cc Jarvik-7 heart, which has been used as an emergency "bridge" without an approved IDE in three patients.

Question 3: Does FDA support the development of a uniform master implant protocol so that useful, consistent scientific information could be obtained from all the centers using a particular device?

Response:
Yes. Since 1985, the Agency has taken steps to assure that the investigation of each model of artificial heart conforms to a uniform protocol, with some allowances made for medical needs and the practices of individual medical centers.

Question 4: How many patients have had heart assist devices inserted? How many of these patients have died before a donor heart became available?

Response:
Twenty-seven patients have had artificial hearts and left ventricular assist devices (LVADs) implanted. Nine patients died while awaiting donor transplants.

Of the 27 implanted devices, 9 were total artificial hearts; 18 were LVADs.

Of the nine patients who died while awaiting a human donor heart, one had received an artificial heart and eight had received LVADs.

Question 5: Has FDA reviewed Symbion's submission following the panel meeting on December 20, 1985? If so, what are the results of that review?

Response:
Yes. FDA staff and the Circulatory System Devices Advisory Panel and its consultants reviewed Symbion's revised protocol for the Jarvik-7 permanent artificial heart. In a letter dated April 18, 1986, FDA approved the protocol, subject to the case-to-case review of future implants, which was recommended by the panel during its December 20 meeting.

Question 6: Has FDA approved the use of the Jarvik-70cc under an Investigational Device Exemption (IDE) yet?

Response:
FDA is reviewing required data only recently submitted by the company requesting this IDE.

Question 7: Why did FDA decide to conduct case-by-case reviews of the next three permanent artificial heart implants?

Response:
The first four recipients of the 100cc Jarvik-7 heart had severe complications involving strokes, renal problems and bleeding. In view of these complications, the panel recommended, and FDA agreed, that the study protocol needed extensive modifications in patient management, device operating parameters, and data collection and analysis. To determine if these changes would improve patient outcome, it was decided that each subsequent implant would be reviewed prior to the initiation of the next one.

Questions 8 and 9: Given that some temporary implants may become permanent, how can FDA ensure that temporary implant patients receive the same protection and rights as patients receiving permanent implants? How does FDA guarantee that the hospital in which a temporary implant has been performed is prepared to handle the possibility of the implant becoming permanent?

Response:
To accommodate the possibility that a "bridge" patient may become a permanent artificial heart recipient, FDA requires that the informed consent forms used at the approved medical centers adequately forewarn patients and their families.

We also require each center to make a written commitment to FDA that they have the staffing and logistics capability to provide long-term care for these patients. This commitment forms a part of the IDE.

Mr. **Volkmer**. We will recess now and return at 3:25.

[Recess.]

Mr. **Volkmer**. The subcommittee will resume.

Since Mr. Norris had to leave, Dr. Mohan, I do have one additional question, and I am sure that you could provide the answer.

Dr. McIntosh, could you let him have that microphone?

That is, as changes take place in one of these devices, whether it's the Jarvik-7 100, or after you have application for an IDE for what we call the mini-Jarvik, or 70 cc, any of these, whether it's a left ventricle device or what, if there are modifications proposed by the manufacturer, what do you require as far as additional testing, that type of procedure, if anything?

Dr. **Mohan**. Mr. Chairman, that depends on the nature of the change to a certain extent. For most significant changes, we do require a supplement to be submitted with the justification for why that change is necessary and whatever scientific data they have regarding, substantiating, why that change is necessary and why it wouldn't affect adversely the safety and effectiveness, of the device.

For minor changes, you know, comparatively less data is required. For example, if there was a change in the heart valve and one were going from one heart valve to another, and both were, let's say, approved heart valves, we wouldn't require too much in terms of testing. But when the changes are significant, for example, to be more specific, when you go from a larger heart to a smaller heart in which the likelihood is that one can't translate the experience of the larger heart totally for the smaller heart, in that case, we would require more data and a fair amount of preclinical work including animal studies.

Mr. **Volkmer**. You would perhaps include animal studies within that, as far as that type of——

Dr. **Mohan**. For those kinds of changes—yes.

Mr. **Volkmer**. Because it's almost a new different instrument then——

Dr. **Mohan**. That's right.

Mr. **Volkmer** [continuing]. From your viewpoint.

But if you're just changing maybe a type of material that was being used and that type of material already had some studies or has properties that are not much different from the properties as far as impacting on the human body and its relations to that, you wouldn't require necessarily additional testing on that?

Dr. **Mohan**. Not necessarily.

The point, Mr. Chairman, is that if there is an open scientific question about a particular change which has not been addressed elsewhere and the evidence is not there, then we would require that data to the extent it's needed to show that change——

Mr. **Volkmer**. And it would be fair to say that for each proposed change you would have to make the decision based on that proposed change, and you can't really make a general statement, complete general statement.

Dr. **Mohan**. That's right.

Mr. **Volkmer**. All right.

Dr. Lenfant, as I understand it, clinical trials of the electrically powered left ventricular assist device—and I believe you have that, one of those devices there, do you not?—is scheduled to begin in 1987. Is that correct?

Dr. **Lenfant**. That's correct, Mr. Chairman.

Mr. **Volkmer**. What information are we expecting to learn from these trials?

Dr. **Lenfant**. Let me backtrack a bit and say that just now we are doing bench testing with the device. Once that is completed and we are satisfied we are dealing with a reliable device on a bench, then we move to the next phase—which is using this device in human clinical applications—and basically assess whether the match of the device and the patient is something which is workable, reliable, and effective.

Mr. **Volkmer**. Is NIH funding any of the clinical evaluation of the pneumatic systems?

Dr. **Lenfant**. No. We have done the—supported the work on the—you are referring to the Jarvik heart?

Mr. **Volkmer**. No, I am talking about the electrically powered—oh, it is the Jarvik, all right. You're not on the Jarvik heart?

Dr. **Lenfant**. The answer to that is no, not for the Jarvik.

Mr. **Volkmer**. All right. And why? Can you tell us why not?

Dr. **Lenfant**. Well, because basically the device moved into clinical applications by decision of the private sector and Dr. DeVries himself. And there was really no consultation between us and Dr. DeVries at that time. And our feeling is that he felt he was ready to do it. Therefore, if the private sector is willing to engage in this kind of activity, we feel that we have no reason to provide support.

Mr. **Volkmer**. In other words, if the private sector starts into it, what I am seeing then, you tell me if the private sector proceeds with something on their own and it progresses to a certain stage, then NIH is not going to come in and help out?

Dr. **Lenfant**. That's correct, especially for clinical applications.

Mr. **Volkmer**. All right.

Well, before I go to full panel questions, I will yield to the gentleman from California for any questions he may have.

Mr. **Packard**. Thank you, Mr. Chairman.

Could I get the name of the doctor again that is replacing Dr. Norris?

Dr. **Mohan**. It is Mohan.

Mr. **Packard**. Thank you very much.

And I am not sure whether this question should be directed to you, Dr. Mohan, or to Dr. McIntosh, whoever you feel would be the most appropriate to answer.

Why does FDA handle these on a case-by-case basis? Is there enough information at the present time to be able to set down some general guidelines that would make the approval process much simpler and perhaps quicker, particularly in the case of emergencies?

Dr. **Mohan**. Let me address that, and I think Dr. McIntosh may want to address it also. Until last December, that is exactly what we had. We had some general guidelines, and we were not doing it on a case-by-case basis for the permanent implant study. The questions that came up regarding the adverse reactions—the strokes, the kidney problems, and so forth, and the concerns that those reactions created were very thoroughly discussed at a panel meeting which we organized last December, at which Symbion and Dr. DeVries made very fine and very exhaustive presentations. As a result of that it was the opinion of our panel that there are enough open questions—this is a very preliminary study—there are enough open questions that on one hand one shouldn't stop the study, and prudence should be exercised. And therefore there should be a closer look at it on a case-by-case basis to see what we did learn from the last experience and what can we do different for the next one to maximize the scientific yield from this investigation and to maximize the benefit to the succeeding patients.

Mr. **Packard**. Does the procedure of authorizing differ in the case of an artificial device from that of a heart transplant? Does FDA get involved in heart transplant approvals on the same basis that they do on artificial devices?

Dr. **Mohan**. No, sir, our law does not require us to get into that.

Mr. **Packard**. Are there—and this probably should be directed to one of the other panel members—but to your knowledge, are there the same kinds of side effects or contraindications—or complications is probably a better word—from a transplant as we find from the devices? In other words, we are not finding now a propensity toward stroke or toward kidney problems or other problems that we are now finding in the devices? Dr. McIntosh and then we'll get to Dr. Lenfant.

Dr. **McIntosh**. That is true. I think the number of patients who come to transplantation are, first of all, an entirely different category of patients. They meet different criteria. All these patients who were implanted with the Jarvik-7 were not transplant candidates, by virtue of age and coexisting diabetes mellitus. So, we are looking at a patient population which may be a little bit younger, that may not have the chronic pulmonary and renal insufficiency that these four patients have had. And one would predict, as Mr. Norris pointed out, that these complications may be a bit more expected, if you will, in this small cadre of four patients. They're all sort of the extremes. And this has sort of been true, I think, of most new devices, most new medicines in the field of medicine, is that, when you start out with a new device, whether it's the use of steroids or the implantation of an artificial valve or a total artificial heart, you really start dealing with the worse-case situations, because there's usually some other modality that we can use to treat those other patients, other medicines, other implantable devices, or what have you.

So, I think that, if you stop and look at the fact that Dr. DeVries and his colleagues have surveyed now about 175 patients, I think, and have selected 4, they are only looking at 2 percent of acceptance and that accept the device, which is pretty close scrutiny, I think, and says something, I believe, about the informed consent from the patient's standpoint as well.

Mr. **Packard**. Dr. Lenfant.

Dr. **Lenfant**. Yes, I just would like to add to the second part of your question, that is, whether there are some similar complications with heart transplants. The complications are not similar, but there are some complications with heart transplant. Basically you have to walk a very thin line between rejection, on the one hand, and infection, on the other hand. One of these complications, rejection, is controlled by drugs such as cyclosporin, which I am sure you heard of. And the administration of that drug is, of course, under the aegis of the Food and Drug Administration for this particular purpose. I don't know if it has passed the experimental phase. I guess it has.

But cyclosporin is a drug which brings about some complications in itself, that is, kidney alterations and in some cases elevation of blood pressure.

Mr. **Packard**. Thank you.

Has the—rather, under what circumstances would FDA deny the use of the artificial heart, knowing or assuming there's no other alternatives and that the patient would die without the use of such device? Under what circumstances would you normally put a hold or a stop on the use of it, particularly in light of clinical experience?

Dr. **Mohan**. That's a difficult one, Mr. Packard. You know, we can't really a priori lay out specific conditions under which, even in an emergency condition, we would say no; that's difficult to do in advance. But what guides us? Well, what are the basic principles that guide us? The way we look at these applications is, we say, is the risk, whatever that risk is to the patient, is the benefit to the patient enough for him to take that risk? Or is the benefit to science in general—and the latter is the secondary point—in general, is enough so that the risk and sacrifice which the patient makes is worth it?

In general terms, that's the kind of balancing we do.

Mr. **Packard**. Is FDA satisfied with the cooperation and the participation that you have received from the makers, the surgeons, the team that is involved in the artificial devices, Jarvik-7 and others perhaps, are you satisified that they are working with and cooperating with FDA in an effort to make certain that they comply?

Dr. **Mohan**. Yes, I believe that they are working in good faith and with due speed and so far in a responsible manner to comply with our requirements. I think the nature of this study, the demands for a lifesaving device under emergency, that this is—as this breakthrough kind of technology unfolds, it points out in the entire system things which we all need to catch up with. And to a certain extent, I think you see some of that, both at the end of the sponsor and the investigator and perhaps at the FDA. We all have a learning process to go through with this technology.

I would, of course, looking at it from FDA's viewpoint, would want that, whatever requirements we have, get satisfied very, very quickly so that we can go through our process and get things in the kind of orderly fashion that we are required to by law so that we don't have to make judgments 2 o'clock in the morning as to whether we should or shouldn't allow a patient who's dying, allow him to be put on an artificial heart. That's not the role that FDA likes to be in.

Dr. **McIntosh**. Mr. Packard, may I respond to that? I feel that Symbion and Dr. DeVries cooperated fully in the preparation of this additional data for that December 20 panel meeting. We had a tremendous charge delivered to us of the panel. That was to try and investigate this device as to whether it was a cause and effect of these complications. And they submitted to us, upon our request, all the data that we have requested, including the transcripts of the 3-day symposium that they had on anticoagulation problems held in Utah. Those materials were then passed on to the panel members. They were asked then to submit questions back to FDA and to me, which we then put in the problematic areas and got back, as we had agreed, to Symbion and to Dr. DeVries 1 week prior to the formal panel meeting.

Mr. **Packard**. What came out of that panel, the panel meeting? What findings did FDA have or make?

Dr. **McIntosh**. Well, the findings that were summarized in the statement were that we would proceed on a case-by-case basis, that we felt that, in reviewing the complications, whether they were device related or management related, the major problem we looked at was stroke. Of the two patients that have had five events or five strokes, three of those were caused by a blood clot, or an embolus, and two were hemorrhagic, or more patient-management related than device related.

The other areas we looked at in terms of renal and pulmonary insufficiency, breakdown of blood cells, infection, and so forth, we did not feel that the device was directly related to those.

But I think at all turns then that certainly they cooperated with us in providing us with the data that we needed to conduct a rather long and rigorous panel meeting on the 20th. And I think it was only because of their cooperation that we were able to come to a decision at the close of that panel meeting.

They have since that time submitted the revised protocol to us as agreed. I have had a chance to review that protocol. The panel will review that and will comment back to the FDA so they can respond within 30 days' time. But I do think that there has been a good spirit of cooperation between the panel, the FDA, Symbion, and Dr. DeVries. And I certainly applaud them for that.

I just assume that, in terms of the IDE that we request for the small, 70cc Jarvik device, that Dr. Jarvik and Symbion will not want to tarnish his sterling record to this point in terms of compliance.

Mr. **Packard**. Is it your hope and plan then that, in view of these findings and as they unfold with additional experience, that the time will come when it will not be necessary to review them on a case-by-case basis, that again we can return to general guidelines and requirements that upon compliance they could move ahead, particularly on an emergency basis?

Dr. **McIntosh**. I think that would be entirely appropriate. I mean, we have to remember that we are still dealing with a very small number of devices. There have only been four——

Mr. **Packard**. I understand.

Dr. **McIntosh** [continuing]. Chronically implanted in this country, three of which have used a certain kind of valve; and one has used a different kind of valve. So, we are looking at small numbers compared to the numbers that we normally look at if we look at heart valves, pacemakers, catheters, and what have you. The magnitude of the study is overwhelming. We look at them and say, there's so much data, we must be able to evaluate this device. But I can tell you as a physician that, having had the opportunity in the early 1970's of having to implant an artificial valve in a patient in which there had been a twenty one-thousandths of an inch engineering change, that we were not informed of in the field, this before the device amendment, that caused a number of deaths across this country, because the ball became lodged and stuck in this device, that I feel that the type of overview that the panel and the FDA has carried out is appropriate to protect these kinds of engineering changes which take place in the laboratory, which don't always translate to the benefit of the patient in whom these devices are implanted.

Dr. **Mohan**. If I may——

Mr. **Packard**. Please.

Dr. **Mohan**. If I may add to that, Mr. Packard, I would just like to clarify something about the case-by-case situation. The only part of this whole thing for which we require a case-by-case review by FDA is for the permanent implants being done by Dr. DeVries. For the bridge-to-transplant use, at the three institutions, 10 apiece, we have given them permission, general guidelines, et cetera. They can do it anytime they want.

Also, I would like to clarify that the guidelines that we have for emergency use of any medical device, what those guidelines require is that for the first use the user can assume that FDA will exercise its enforcement discretion and not take action against them. And the hope is that after the first use, the scientific data, the IDE application, et cetera, will come in. And FDA would then be part of the picture, and then decisions would be made after that.

Mr. **Packard**. Thank you.

We have heard testimony today, as you have, recommending an umbrella institutional review board. Would you feel that that would serve any useful purpose in light of FDA's responsibility?

Dr. **Mohan**. Again, this is the first time I had heard of that proposal as such, so I will give you an off-the-cuff kind of a personal reaction. Very frankly, no. I think we have fairly adequate regulatory mechanisms within FDA. We have our advisory panel, on which we can get people with all kinds of expertise, to help us in resolving questions. I don't think we need another level of regulation.

Mr. **Packard**. Thank you.

Thank you, Mr. Chairman.

Mr. **Volkmer**. Dr. McIntosh and Dr. Lenfant, I have a question. Looking to the future, let's assume that fiscal year 1987, both the 100 cc and the 70 cc, pass all tests. And people start living maybe on the sixth and the seventh one 1½ years, 2 years. And we have very few strokes. And they are ambulatory and everything else is going great. And sometime in the future they are approved for marketing. Now, the question I have is, what are the costs going to be, and who is going to pay for it? Because on permanent transplants right now, we only have, you know, the ones being done at Humana; and we know who's paying for those. Those costs are running astronomical. I am sure some of those costs will be able to come down as we do it. But who's going to pay for it?

Dr. **Lenfant**. Well, I don't know who is going to pay for it, but I can tell you how much it is going to cost. In this study here, that aspect of the artificial heart was considered quite carefully. The estimate, and you heard some figures today, is that there may be some 20 to 30,000 people a year who might be recipients of the chronic artificial heart. Although the cost, as you heard it from Dr. DeVries, is high today, there is an expectation that eventually it would go down to probably $150,000 a patient, for about a 2-year survival.

Now, if we multiply that by the number of patients, we are reaching an amount per year of $2.5 to $3 billion, which is, of course, a sizable amount of money. Who is going to provide that money, it is not mine to say. I might only repeat what was indicated in this report, that there are today some similar long-term therapies which are in the same order of cost.

Mr. **Volkmer**. Renal dialysis, which is——

Dr. **Lenfant**. For ——

Mr. **Volkmer** [continuing]. That costs, and the Federal Government is picking up a large chunk of that.

Dr. **Lenfant**. Yes; I surmise. I don't know for sure, but I surmise.

Mr. **Volkmer**. So, that isn't part of the study, where the money is going to come from to pay for it.

Dr. **Lenfant**. I——

Mr. **Volkmer**. I mean, there's not——

Dr. **Lenfant**. All I can tell you——

Mr. **Volkmer**. There's not very many individuals, there are some in this country, but not very many individuals that are going to be able to come in and plunk down $100,000 or $150,000 for a permanent artificial heart transplant. We have to recognize that.

The second question is the question about, what about the insurance carriers, whether they would do it. And if they do it, I'll guarantee you everybody's premiums are going to go up some.

Dr. **Lenfant**. Well, I am not in a position to answer that question either personally or on behalf of the——

Mr. **Volkmer**. Does anybody else wish to comment on it at all?

Dr. **McIntosh**. I think you're absolutely right. In the beginning, the transplantation procedures, the heart, were not covered by insurance, and they are now. If it realistically comes down to a price equivalent to a transplant, then I think the question becomes perhaps a little less important. If we can put an artificial heart in somebody for the same price that we can transplant somebody, that may be a key issue. And I don't know the answer to that.

Mr. **Volkmer**. Dr. Lenfant, in your study we don't get that far down, do we?

Dr. **Lenfant**. No, we don't.

Mr. **Volkmer**. I have one that I asked the staff to make sure I didn't forget, and then I did forget.

Dr. Lenfant, Gramm-Rudman, 4.3 percent reduction, March 1, approximately 20, 25 percent reduction, October 1 for the following year. What does that do to all these programs and all these devices that you have here and others?

Dr. **Lenfant**. Well, I think it's premature for me to answer this question, Mr. Chairman. As you saw from the documentation that we submitted to the committee, the Institute has been providing approximately $12 million a year to this program for a number of years. We feel that it is an adequate and appropriate amount of money. If nothing was to change today, we would probably not change that allocation either up or down.

With the implementation of Gramm-Rudman legislation and the President's budget, I don't know what we are going to do relative to this particular program. It is premature for me to answer that question.

But I would like to submit to the committee that our Institute has many, many priorities. This one, the priority of this program, is not the lowest; but it's not the highest, as well. So, therefore, with our national advisory council and all the experts in the field who are advising us, we will try to do the best we can.

Mr. **VOLKMER**. I am assuming everybody in the Government, I hope, will do the best they can. But still it would have an impact on some of the programs if you do receive, let's say, a reduction next year in funding for all your programs of $3 million.

Dr. **LENFANT**. I think it is quite reasonable to assume that this one will have to participate in this reduction.

Mr. **VOLKMER**. Dr. Mohan, FDA, if you receive a reduction next year of 20 to 25 percent in funding to administer these programs and have a review, et cetera, of these programs, how does that impact on the programs?

Dr. **MOHAN**. It's a little difficult to anticipate exactly what might happen. Again, those decisions are being made in the agency right now. But given the overall priorities which Commissioner Young has set forth in his action plan, for example, product approval, it is a very high priority item.

Mr. **VOLKMER**. So, you would be impacted less than perhaps other things within FDA?

Dr. **MOHAN**. Well, as head of my program, I would hope so.

Mr. **VOLKMER**. I have no further questions. I want to thank all of this panel also. You were very good witnesses and have been very informative and helpful.

I think it has been a very good hearing. Before we adjourn, I would like to recognize the gentleman from California with a short statement.

Mr. **PACKARD**. Thank you. I simply wanted to also congratulate the witnesses. I think that the testimony has been outstanding. It has been a very interesting and informative hearing. I think it will certainly help us make some conclusions relative to our involvement as well as our reaction to the experiments that are going on.

I certainly believe there has to be an ongoing assessment of risk versus benefit. And I think that is being adequately done. I think it can continue to be adequately done by the private sector as well as the regulatory agencies that are involved in this program. My personal feeling before as well as after the hearing is that it would be irresponsible and perhaps bordering on criminal negligence to actually abandon the process or the experimentation. I think it ought to go forward, recognizing that the safety to the patients and to society generally ought to be addressed very carefully, as I think we have been.

Thank you very much.

Mr. **Volkmer**. Thank you.

The subcommittee will stand adjourned.

[Whereupon, at 4 p.m., the subcommittee was adjourned, subject to the call of the chair.]

APPENDIX 1

Table 1. Tabulation of Clinical Use of Mechanical Circulatory Support Devices for Bridge to Transplant and Permanent Application (continued)

Patient Description/ Name	Implant Date	Implant Site/ PI	Device Used	Mechanical Pumping Duration	Clinical Use	Medical Indications	Complications	Outcome
52 yr. old male/ William Schroeder	11/25/84	Humana Hospital-Audobon Louisville, KY/ Dr. W. DeVries	Jarvik-7 TAH	continuing	Permanent implant	Cardiomyopathy	Pulmonary insufficiency, 3 strokes, initial one 12/13/84, Post-op bleeding	Living to date
58 yr. old male/ Murray Haydon	2/17/85	Humana Hospital-Audobon Louisville, KY/ Dr. W. DeVries	Jarvik-7 TAH	continuing	Permanent implant	Cardiomyopathy	1 stroke, Post-op bleeding, requires respirator	Living to date
33 yr. old male/ Thomas Creighton	3/6/85	University Med. Ctr., Tucson/ Dr. Jack Copeland	Phoenix Heart TAH	12 hours	Bridge to transplant	Viral cardiomyopathy	Pulmonary edema, extended time on heart lung machine, bleeding, stroke	Died 3/8/85, pulmonary hypertension
16 yr. old male/ Michael Jones	3/24/85	Jewish Hospital, Louisville/ Dr. L. Gray	Pierce-Donacky Biventricular assist made by Thoratec	4 days	Bridge to transplant	Acute viral cardiomyopathy, severe heart failure and respiratory failure	Acute renal failure requiring dialysis through 5/28/85, respiratory insufficiency, was on respirator until 6/22/85, gall bladder disease, developed CMU, required physical rehabilitation	Alive and doing well
39 yr. old male/ Terrance Kelly	4/3/85	Stanford Univ. Med. Ctr./ Dr. P. Oyer	Novacor 100 LVAS	16 days	Bridge to transplant	End-stage ischemic heart disease	No device related complications, renal failure requiring dialysis, hepatic dysfunction	Death 16 days after transplant, bilateral fungal pneumonia

Table 1. Tabulation of Clinical [illegible] of Mechanical Circulatory Support Devices for Bridge to Transplant and Permanent Application

Patient Description/ Name	Implant Date	Implant Site/ PI	Device Used	Mechanical Pumping Duration	Clinical Use	Medical Indications	Complications	Outcome
47 yr. old male/ Mr. Karp	4/4/69	Texas Heart Inst./ Dr. D. Cooley	Liotta TAH	63 hrs.	Bridge to transplant	Heart failure, unable to wean from CPB	Anatomical fit	Died 1 day after receiving transplant
21 yr. old male	2/9/78	Texas Heart Inst./ Drs. Norman/Cooley	Thermo Electron Model 7 ALVAD	5+ days	Bridge to transplant	Post cardiotomy stone heart syndrome, acute bacterial endocarditis	Acute tubular necrosis of native and transplanted kidneys	Died 15 days after transplant from gram-negative sepsis
male/Wille Brordus Meuffels	7/23/81	Texas Heart Inst./ Dr. Cooley	Akutzu TAH	54 hrs.	Bridge to transplant	Post cardiotomy, unable to wean from CPB	Used IAB, TAH on day 1; on day 2 used ECMO. anatomical fit	Died of heart rejection 8 days after transplant
61 yr. old male/ Dr. Barney Clark	12/2/82	University Hosp. Univ. of Utah/ Dr. W. DeVries	Jarvik-7 TAH	112 days	Permanent implant	Cardiomyopathy	Broken valve, seizures	Died on 112th day
52 yr. old male/ Joseph Zagorsky	2/3/83	St. Louis Univ./ Dr. G. Pennington	ECMO	3 days	Bridge to transplant	Acute cardiogenic shock	Sepsis	Died 1 month after receiving transplant
25 yr. old male/ Kenneth Bray	7/16/83	St. Louis Univ./ Dr. G. Pennington	ECMO	5 days	Bridge to transplant	Acute myocarditis cardiogenic shock	Sepsis, pulmonary infarcts	Died 1 day after receiving transplant
51 yr. old male/ Robert St. Laurent	9/5/84	Stanford Univ. Medical Center/ Dr. P. Oyer	Novacor 100 LVAS	8.5 days	Bridge to transplant	End-stage ischemic disease, cardiac tamponade	No device related complications	Transplanted, discharged and doing well
47 yr. old male/ Ronald Mecham	9/6/84	Pacific Presbyterian Medical Center, S.F./ Dr. J.D. Hill	Pierce-Donachy Biventricular assist made by Thoratec	52 hrs.	Bridge to transplant	Post myocardial infarction, cardiogenic shock	Lost leg due to IAB left diaphram paralysis which was resolved, mild episode of infection, acute renal failure	Transplanted, discharged from hospital 12/20/84 and doing well

Table 1. Tabulation of Clinical [illegible] Mechanical Circulatory Support Devices for Bridge to Transplant and Permanent Application (continued)

Patient Description/ Name	Implant Date	Implant Site/ PI	Device Used	Mechanical Pumping Duration	Clinical Use	Medical Indications	Complications	Outcome
53 yr. old male/ Lief Stenberg	4/10/85	Karolinska Hosp. Stockholm, Sweden Dr. Semb	Jarvik-7 TAH	226 days	Permanent implant	Cardiomyopathy	Stroke	Died 11/21/85
62 yr. old male/ Jack Burcham	4/15/85	Humana Hosp. Louisville,KY/ Dr. W. De Vries	Jarvik-7 TAH	10 days	Permanent implant	Cardiomyopathy	Bleeding, anatomical fit cardiac tamponade kidney dysfunction	Died 10 days after
54 year old male/ Donald Croskrey	5/14/85	St. Louis Univ. Dr. G. Pennington	Pierce-Donachy Biventricular assist pumps made by Thoratec	36 hours	Bridge to transplant	Acute myocardial infarction	none	Transplanted, at home doing well
24 year old female/ Brenda Parr	7/21/85	Milton S. Hershey Med Center/Pa. State Univ./ Dr. W. Pierce	Pierce-Donachy Biventricular assist pumps	3 weeks	Bridge to transplant	End stage cardiomyopathy, presumed viral	none	Transplanted on 8/11/85 and is home doing well
25 year old male/ Michael Drummond	8/29/85	University Medical Center, Tucson Dr. Jack Copeland	Jarvik-7 TAH	9 days	Bridge to transplant	Viral cardiomyopathy	Pulmonary edema during implant period, embolic strokes	Transplanted on ninth day, discharged and doing well
44 year old male/ Anthony Mandia	10/18/85	Pa. St. Hershey Medical Center Dr. W. Pierce	Penn St. TAH	11 days	Bridge to transplant	Acute congestive cardiomyopathy	Metabolic encephalopathy	Died 7 days after transplant of fungal sepsis
42 year old female/ Linda Underwood	10/22/85	St. Louis Univ./ Dr. G. Pennington	Pierce-Donachy Biventricular assist pumps made by Thoratec	9 hours	Bridge to transplant	Cardiogenic shock from post partum cardiomyopathy	Bleeding	Transplanted, at home doing well

, Table 1. Tabulation of Clinical . of Mechanical Circulatory Support Devices for Bridge to Transplant and Permanent Application (continued)

Patient Description/ Name	Implant Date	Implant Site/ PI	Device Used	Mechanical Pumping Duration	Clinical Use	Medical Indications	Complications	Outcome
47 year old male/ Thomas Gaidosh	10/24/85	Presbyterian-Univ. Hosp., Pittburgh/ Dr. B. Griffith	Jarvik-7 TAH	4 days	Bridge to transplant	Cardiogenic shock with cardiomyopathy	none	Transplanted doing well
male/ Richard Dalara	10/25/85	Pacific Presbyterian Medical Center, S.F./ Dr. D. Hill	Pierce-Donachy Bi-Ventricular assist made by Thoratec	87 hours	Bridge to transplant	Cardiomyopathy	Mild rejection	Alive and well
27 year old female/ Glena Walker	10/30/85	Jewish Hosp. Louisville,KY/ Dr. L. Gray	Pierce-Donachy Bi-Ventricular assist made by Thoratec	15 hours	Bridge to transplant	Congestive cardiomyopathy	DIC Severe pulmonary hypertension, acute renal failure requiring dyalysis/ hypertension	Died 12/31/85
40 year old female/Mary Lund	12/18/85	Abott Northwestern Hosp., Minneapolis Heart Inst./ Dr. L. Joyce line	Modified Jarvik-7 TAH	45 days	Bridge to transplant	Failing heart muscle and resulting hypoperfusion	Ischemic leg following IABP. Superficial drive-line infection	Transplanted 1/31/86, alive doing well
53 year old male	1/9/86	Horley Street Clinic, England/ Dr. B. Glenville	Pierce-Donachy LVAD, made by Thoratec	12 hours	Bridge to transplant	CABG Reoperation, Patient had series of complications following initial CABG 3 mo. earlier	Initial biventricular failure for 3 hours followed by right side recovery	Alive, doing well
47 year old male	1/19/86	Texas Heart Inst., Houston, TX/ Dr. O. H. Frazier	Thermedics Model 14-B LVAD	Continuing	Bridge to transplant	Cardiomyopathy	None to date	Awaiting transplant, doing well

Table 1. Tabulation of Clinical Use of Mechanical Circulatory Support Devices for Bridge to Transplant and Permanent Application (continued)

Patient Description/ Name	Implant Date	Implant Site/ PI	Device Used	Mechanical Pumping Duration	Clinical Use	Medical Indications	Complications	Outcome
30 year old male/ Joseph Burello	2/2/86	Presbyterian-University Hosp./ Dr. B. Griffith	Jarvik-7 TAH	Continuing	Bridge to transplant	Cardiogenic shock following M.I. with IABP and dual ventricular support with Biomedicus blood pump	None related to implant, Patient has pre-existing lung injury related to acute pulmonary edema and probable pulmonary emboli (not thought to be related to A.H.)	Alive, improvement in pulmonary status so that heart transplant can be done
40 year old female/ Bernadette Chayrev	2/3/86	University Med. Center, Tucson/ Dr. J. Copland	Modified 70cc Jarvik-7 TAH	Continuing	Bridge to transplant	Multiple Organ failure, rapidly determining viral myocarditis	Transplanted but donor heart failed. Second TAH implanted, mild pulmonary edema	Alive, awaiting second transplant
41 year old male/Kent Hall	2/3/86	Texas Heart Inst., Houston/ Dr. O.H. Frazier	Jarvik-7 TAH	Continuing	Bridge to transplant	Cardiomyopathy	Bleeding (corrected)	Alive and stable awaiting transplant

APPENDIX 2

2/5/86

SUMMARY OF CLINICAL USE OF MECHANICAL CIRCULATORY SUPPORT DEVICES FOR BRIDGE TO TRANSPLANT AND PERMANENT APPLICATIONS

Clinical Use	Total Attempts	Survival to Date	Waiting for transplant
Permanent Implant (TAH)(1)	5	2	N/A
Bridge to Transplant			
ECMO	2	0	-
TAH(2)	10	6	3
LVAD(3)	5	3	1
BVAD(4)	7	6	0
Subtotal	24	15	4
Total	29	17	4

(1) All Jarvik-7 TAH devices

(2) One Liotta TAH, no survivor
One Akutzu TAH, no survivor
One Phoenix TAH, no survivor
Six Jarvik-7 TAH patients (2 modified 70cc), six survivors, three awaiting transplan
One Penn. St TAH, no survivor

(3) One Thermo Electron Model 7 ALVAD, no survivor
Two Novacor 100, LVAD one survivor
One Pierce-Donachy LVAD/Thoratec, one survivor
One Thermedics Model 14-B LVAD, one survivor awaiting tranpslant

(4) Seven Pierce-Donachy BVAD/Thoratec, six survivors

APPENDIX 3

CLINICAL EXPERIENCE WITH THORATEC VAD (28-JAN-86. FARRAR)

CASE	CENTER	PT	SURGEON	DATE	AGE	SEX	BSA	WT	HT	PUMP	Use	Hours	Rslt	IN	OUT	SURV
1982																
1	St. Louis	1	Pennington	30-Mar-82	71	M				LVAD		3		LA	Ao	
2	St. Louis	2		30-Apr-82	27					LVAD				LA	Ao	
3	PMC	1	Hill	05-May-82	60	M	1.80	73	164	LVAD	SK-WFB	67		LA	Ao	
4	St. Louis	3		26-May-82	50	M				RVAD		120	Dis	RA	PA	1
5	St. Louis	4		25-Jun-82	57	M				RVAD		3		RA	PA	
6	St. Louis	5		28-Jun-82	69	M				BVAD		288	Wean	LA	Ao	
7	St. Louis	6		01-Jul-82	71	M				LVAD		3		LA	Ao	
8	PMC	2	Hill	07-Sep-82	66	M		101		LVAD	WFB	1		LA	Ao	
9	St. Louis	7		27-Sep-82	32	M				LVAD				LA	Ao	
10	St. Louis	8		08-Oct-82	55	M				RVAD		96	Dis	RA	PA	2
11	St. Louis	9		01-Nov-82	15	F				LVAD		3		LA	Ao	
12	St. Louis	10		01-Dec-82	51	F				LVAD		9		LA	Ao	
13	PMC	3	Hill	02-Dec-82	60	M	2.10	89	179	LVAD	WFB	304		LA	Ao	
1983																
14	PMC	4	Hill	23-Feb-83	73	M	1.83	65		RVAD	WFB	2		RA	PA	
15	St. Louis	11		26-Feb-83	60	M						3				
16	St. Louis	12		20-Mar-83	60	F				LVAD		48		LA	Ao	
17	PMC	5	Hill	30-Mar-83	53	M	1.87	78	168	LVAD	WFB	37		LA	Ao	
18	St. Louis	13		13-May-83	63	F				LVAD		3		LA	Ao	
19	St. Louis	14		07-Jul-83	28	F				BVAD		216	Dis	LA	Ao	3
1984																
20	PMC	6	Hill	03-Jan-84	72	F	1.66	59		LVAD	WFB	288		LA	Ao	
21	St. Louis	15		13-Jan-84	61	M				LVAD		72	Dis	LA	Ac	4
22	St. Louis	16		15-Feb-84	60	M				LVAD		72	Dis	LA	Ao	5
23	St. Louis	17		22-Feb-84	58	M				BVAD		8				
24	Mayo	1	Ceithaml	29-Feb-84	41	M	2.14	95		LVAD	WFB	24		LA	Ao	
25	St. Louis	18		12-Mar-84	48	M				LVAD		67	Dis	LA	Ao	6
26	St. Louis	19		02-Apr-84	45	M				BVAD		64	Dis	LA	Ao	7
27	Genolier	2	Lichsteiner	13-Apr-84	41	M				LVAD	WFB	24		LA	Ao	
28	Kettering	1	Zwart	23-Apr-84	59	F	2.04	96	165	LVAD	WFB	71	Wean	LA	Ao	
29	Mayo	2	Downing,Plu	16-May-84	48	M	1.86	77		LVAD	WFB	5		LA	Ao	
30	Genolier	1	Lichsteiner	07-Jun-84	17	F				LVAD	WFB	168	Wean	LA	Ao	
31	PMC	7	Hill	14-Jul-84	66	F				RVAD	WFB	139	Wean	RA	PA	
32	St. Louis	20		31-Jul 84	64	F				BVAD		3		LA	Ao	
33	St. Louis	21		31-Jul-84	67	M				LVAD		144	Wean	LA	Ao	
34	Mayo	3	Schaff	17-Aug-84	21	F	1.28	39	150	LVAD	WFB	3		LA	Ao	
35	St. Louis	22		22-Aug-84	41	M				BVAD		20		LA	Ao	
36	PMC	8	Hill	06-Sep-84	47	M	2.02	76	185	LVAD	SK-BR	52	Trns	LV	Ac	8
37	St. Louis	23		13-Sep-84	49	M				BVAD		6				
38	Kettering	2	Zwart	26-Sep-84	40	F	1.56	48	162	LVAD	WFB	24		LV	Ao	
39	Michigan	1	Kirsh,Long	20-Nov-84	57	M	1.90	85	165	LVAD	WFB	30		LA	Ao	

WFB - Weaning of bypass!

SK-WFB Shock

CLINICAL EXPERIENCE WITH THORATEC VAD (26-JAN-86, FARRAR)

CASE	CENTER	PT	SURGEON	DATE	AGE	SEX	BSA	WT	HT	PUMP	Use	Hours	Rslt	IN	OUT	SURV
1985																
40	St. Louis	24		16-Jan-85	56	M				LVAD	WFB	312	wean	LA	Ao	
41	Mayo	4	Schaff	21-Jan-85	66	M	2.04	83	183	LVAD	WFB	1		LA	Ao	
42	Mayo	5	Pluth	22-Mar-85	62	M	2.10	88	176	BVAD	WFB	2		LA	Ao	
43	Jewish	1	Gray	28-Mar-85	16	M	1.44	45	160	BVAD	BR	120	Trns	LA	Ao	9
44	St. Louis	25		14-May-85	57	M				LVAD	SK-BR	36	Trns	LV	Ao	10
45	St. Lukes	1	Vaughn	27-May-85	53	M				LVAD	Reject	1				
46	St. Louis	26		13-Jun-85	50	M				BVAD	SK-BR	504		LV	Ao	
47	St. Lukes	2	Vaughn	20-Jun-85	52	M	1.97	78	178	LVAD	WFB	51				
48	Kettering	3	Zwart	23-Jun-85	57	M	1.96	84	171	LVAD	WFB	50	Dis	LA	Ao	11
49	St. Louis	27	McBride	30-Jul-85	45	M	1.90	71	178	BVAD	SK-BR	96		LV	Ao	
50	Good Sam	1	Bozorgi	08-Aug-85	47	F	1.73	61	173	LVAD	WFB	120		LA	Ao	
51	PMC	9	Hill	01-Oct-85	53	F		52		RVAD	RVF	213	wean	RA	PA	12
52	PMC	10	Hill	11-Oct-85	52	M		60		BVAD	SK-BR	1		LV	Ao	
53	St. Louis	26	McBride	22-Oct-85	41	F				LVAD		9	Trns	LV	Ao	13
54	PMC	11	Hill	25-Oct-85	33	M				BVAD	BR	87	Trns	LV	Ao	14
55	Jewish	2	Gray	30-Oct-85	27	F	1.75	71	168	BVAD	CM	19		LA	Ao	
56	Aachen	1	Bardosh	07-Nov-85	50	M				LVAD						
57	Kettering	4	Zwart	12-Nov-85	44	M	1.68	75	173	LVAD	WFB	54	Dis	LA	Ao	15
58	Augusta	1	Zumbro	12-Dec-85	45	M				BVAD	CM					
59	Jewish	3	Gray	18-Dec-85	45	M	2.1	88	180	LVAD	WFB	8		LA	Ao	
60	Augusta	2	Zumbro	31-Dec-85	62	F				LVAD	WFB		wean			
1986																
61	Augusta	3	Zumbro	05-Jan-86	56	F				BVAD	WFB					
62	London	1	Glenville	09-Jan-86	53	M				LVAD	WFB-Br	12	Trns			
63	Augusta	4	Zumbro	10-Jan-86	73	F				LVAD	WFB					
64	PMC	12	Hill	21-Jan-86	53	M				RVAD	RVF	168		RA	PA	
65	Milwaukee	1	Galbraith	27-Jan-86	35	M				BVAD	CM			LV	Ao	
66			Competition													
				avg	49		1.70	69	147			74				

Bridge
Cardiomyopathy

4 day X-Plant

LONG TERM SURVIVORS

	YES	NO		%
1982	2	11	2/13	15
1983	1	5	1/6	17
1984	5	15	5/20	25
1985	7	14	7/21	33
1986				
total	15	45	15/60	25

41 LVAD
7 RVAD
17 BVAD

65 total

17 weaned
10 Recovered
6 Transplanted

16 Long term survivors

APPENDIX 4

should not try to regulate these differences away by applying a single formula to all cases. In the President's State of the Union message on February 4, 1986,[5] he described the family and community as "the moral core of our society, guardians of our values and hopes for the future." This rhetoric would seem to be especially applicable in the treatment of sick infants, but it is oddly belied by the regulations of the same administration. Although it is laudable for a government to be concerned about the lives of its vulnerable citizens, life-and-death decisions are made daily in all areas of medicine. The government simply cannot ensure that every one of them is correct — even if it could define correctness — without harming the very citizens it is trying to protect. The best we can hope for is that decisions about the treatment of handicapped newborns are individualized, carefully weighed, and loving. Such decisions are more likely to come from parents and physicians than from the government.

Marcia Angell, M.D.

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ARTIFICIAL HEARTS — PERMANENT AND TEMPORARY

A little more than three years ago, at the University of Utah in Salt Lake City, Dr. William DeVries implanted a Jarvik-7 artificial heart in a 61-year-old patient named Barney Clark. The patient lived 112 days with the device before succumbing to renal failure, infection, and pseudomembranous colitis.[1] His stormy clinical course had been marked by seizures and episodes of mental confusion, recurrent acute tubular necrosis, postoperative subcutaneous emphysema due to ruptured pulmonary blebs, and sudden congestive heart failure due to a fractured mitral-valve prosthesis (which necessitated emergency replacement of the prosthetic left ventricle on the 13th postoperative day).

Since moving to Louisville, Kentucky, Dr. DeVries has placed implants in three more patients, William Schroeder, 52, Murray Haydon, 59, and Jack Burcham, 62. (I identify them because the intense publicity surrounding this work has made their names household words.) None of these patients has yet been described in the medical literature, but the press has told us a great deal about their clinical courses. As of this writing, approximately 15 months postoperatively, Mr. Schroeder is still alive but he has been incapacitated by a series of thromboembolic strokes. Mr. Haydon is also still alive, approximately one year postoperatively, but he has also had at least one stroke, and he remains confined to the hospital, where he requires intermittent assisted ventilation. Mr. Burcham, the last of the series, died of an internal hemorrhage 10 days after the initial operation. A fifth patient, a 53-year-old man, received a Jarvik-7 artificial heart at the Karolinska Hospital in Stockholm last year. He survived for 229 days, but died after a massive stroke.

In other words, three of the first five patients receiving the Jarvik-7 as a permanent heart replacement are dead, two are seriously disabled, and none (except perhaps the Swedish patient) have enjoyed even a few months of life outside the hospital. This is a sobering record. It contrasts starkly with the almost euphoric atmosphere initially generated by the press, particularly when Dr. DeVries moved to Louisville and resumed his work under the exuberant sponsorship of Humana, Inc.

After some hesitation, the Food and Drug Administration has recently given the Louisville team permission to do at least one more permanent artificial heart implantation. Yet most experts now believe that the time has come to call a moratorium on any further use of the Jarvik-7 as a permanent prosthesis, stating that the problem of thrombogenesis on the blood-contacting surfaces of the device should be solved before additional long-term clinical trials are justified. Some experts also believe that resumption of clinical trials should await the development of a more compact, portable or implantable power source, which would allow the patient a better quality of life.

I agree with these experts that we ought not to use the Jarvik-7 for further permanent implants. However, despite the good arguments against any further work on artificial hearts,[2] I still believe that laboratory research on this problem should continue. Heart transplantation offers a much better therapeutic alternative at present, but the number of potential donor hearts will not nearly meet the need for cardiac replacement. Advances in the prevention and treatment of heart disease will undoubtedly reduce that need in the future. However, we cannot expect to eliminate intractable heart failure any time soon, and there will almost certainly continue to be many patients who could benefit from an artificial heart suitable for permanent implantation.

Since we do not yet have such a device, what about using the Jarvik-7 or other types of cardiac prostheses for *temporary* support of patients awaiting cardiac transplantation? This issue of the *Journal* contains a remarkable report by Hill and co-workers[3] of the successful use of a prosthetic left ventricle in a 47-year-old man who had cardiogenic shock after massive myocardial infarction and could not be maintained with pharmacologic support and an intraaortic balloon pump. The artificial ventricle functioned for two days, after which the patient received a heart transplant. He is now doing well after more than a year with his transplant. This is apparently the first detailed medical report of a case of this kind, but the press has recently carried accounts of similar cases being tried in institutions around the country. In one case, a Jarvik-7 heart was in place for 45 days before transplantation was carried out; in another, a young woman received a second artificial heart after her heart transplant failed. The FDA seems willing to approve (or countenance) more widespread temporary use of prosthetic devices, even though it has serious reservations about their permanent implantation.

Annas[4] argues cogently against the strategy of using an artificial heart as a temporary bridge to transplantation. "As long as there is a shortage of transplantable human hearts," he says, "temporary artificial hearts cannot increase the total number of human heart transplants performed; they can only change the identity of the individuals who receive them." Hill et al. acknowledge this point, but counter that "it is arbitrary to assign a higher priority to candidates for elective transplantation." Furthermore, in response to a different argument, that an implant procedure may compromise a patient's chances for subsequent successful transplantation, they add: "there are no data to indicate that carefully chosen patients undergoing transplantation after a bridge procedure will have a substantially poorer prognosis." Hill and his colleagues may be right, but I am not convinced; the ethical argument is a standoff, and the technical issue can only be settled by carefully controlled clinical experience.

That is why I think it is reasonable for the FDA to allow continued clinical experimentation with *temporary* artificial hearts. However, it is important that these trials be limited to a few research institutions where personnel and facilities are available to carry out careful clinical studies and the necessary surgery can be done safely. The FDA should take the initiative in organizing a multicenter trial with established protocols and full reporting of results. In the absence of protocols and cooperation among institutions, we are likely to see a proliferation of competing and unplanned efforts that will not advance the field and may even set it back. It would indeed be unfortunate if the unregulated use of "temporary" artificial heart implants were to result in unintended "permanent" implants.

Research on artificial hearts should be pursued vigorously, even as we concentrate on the prevention and treatment of heart disease and attempt to improve the procurement of heart donors and the survival of transplants. The development of a safe and tolerable permanently implantable prosthesis is evidently still a long way off, but let us hope that federal support of the necessary basic research will continue. Meanwhile, carefully controlled clinical trials should be undertaken to determine how, if at all, temporary use of the available models can be advantageously combined with heart transplantation.

ARNOLD S. RELMAN, M.D.

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4. Annas GJ. No cheers for temporary artificial hearts. Hastings Cent Rep 1985; 15(5):27-8.

CORRESPONDENCE

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HUMAN PARVOVIRUS INFECTION

To the Editor: In the article by Plummer et al. (July 11 issue),* the authors established a relation between an exanthematous disease and a parvovirus. In my opinion, however, they did not show that the disease was indeed erythema infectiosum or the "fifth disease" that those of us in practice have recognized clinically for many years.

It is true that what we have called "erythema infectiosum" is benign and that the rash can come and go for several weeks. But, as Plummer et al. themselves pointed out, only 1 of their 19 patients had the typical "slap sign" or lacy reticular rash that we expect to see, almost invariably, in order to make the clinical diagnosis.

The disease also has a typical sequence of eruption; the facial "slap sign" rash precedes the body rash, and it may even be gone when the body rash appears (or by the time the patient appears in the doctor's office). In addition, the lacy rash on the body characteristically appears not on the "arms and thorax" but on the arms (especially the upper arms), the thighs, and the buttocks. Lastly, the rash does not characteristically involve the palms and soles (Plummer et al. also mentioned this).

To be more convincing, Plummer et al. should find the parvovirus in my kind of erythema infectiosum.

ALAN S. ZISMAN, M.D.
Spring Valley, NY 10977
Hillcrest Medical Center

*Plummer FA, Hammond GW, Forward K, et al. An erythema infectiosum-like illness caused by human parvovirus infection. N Engl J Med 1985; 313:74-9.

To the Editor: In the July 11 issue, Plummer et al. and Dr. Whitley[1] discussed the relation between human parvovirus infection and erythema infectiosum-like illness.

We would like to describe briefly our study of an epidemic of erythema infectiosum-like illness (in which the clinical symptoms were a "slapped-cheek" appearance and a lacy reticular rash on the extremities) between February 27 and March 23, 1982, in the chil-

APPENDIX 5

ADDITIONAL STATEMENT FOR THE RECORD

TESTIMONY

-of-

Mrs. Barney B. Clark

-to-

THE SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT
OF THE COMMITTEE ON SCIENCE AND TECHNOLOGY

I regret being unable to attend and testify in person before this Subcommittee on "Investigations and Oversight of the Committee on Science and Technology" regarding the use of, and the review of technology used to date in the artificial heart implants. However, I appreciate the opportunity to submit my written testimony.

Having no scientific nor medical expertise on this technology, I believe I can best serve the purpose of this committee by relating some pertinent facts with regard to the way in which Dr. Clark became aware of the artificial heart, his investigation of it, what influenced him to volunteer and how he, and our family, felt about that decision once made and the heart implanted.

Dr. Clark became a victim of Cardiomyopathy myocarditis in 1979. In spite of the excellent and aggressive medicinal regime prescribed by his cardiologist, and Dr. Clark's strict adherence to it, by early October, 1982 his heart condition had deteriorated to a point where he had great difficulty walking a very short distance, was totally exhausted all the time and literally fought for breath oftimes at bedrest. We investigated the possibility of a donor heart transplant, but were denied on the grounds that at that particular time, transplants were not available to persons over 50 years of age---Dr. Clark was then 59.

Because the last of the then-proven drugs had become ineffective in stimulating his heart muscle, we were referred to Dr. Jeffrey Anderson in Salt Lake City to try an experimental drug called Amrinone. Dr. Clark's system could not tolerate this drug and it had to be abandoned. Dr. Anderson, then realizing we had no other alternative, referred us to Dr. Wm. DeVries at the Utah Medical Center. It was then we first met Dr. DeVries, received extensive and accurate information regarding the artificial heart, were provided with a copy of the "Consent Form" to study, and were escorted, by Dr. DeVries, through the animal surgery facility where we observed the implanted animals and studied the results of the animal research conducted over the past 15 years. Dr. DeVries informed us they had accomplished all they could through animal experimentation and were screening for a suitable volunteer to receive the artificial heart implant.

We did not agonize over our decision. Dr. Clark had had some medical training himself, had a cardiologist who was totally "up-front" with him and was well aware of his critical physical condition. He had long-since faced reality regarding his mortality and concluded that if he were to receive help, it would be through the artificial heart. Also, he felt he owed a debt to those who had proven the drugs that had kept him alive for three years after the onset of his illness, that he met the rigid requirements of the protocol for the implant and that regardless of whether or not he received personal benefit, there undoubtedly would be much learned that would benefit the medical world and future heart patients. He confided in me that he felt he would be somewhat dissatisfied with himself as a human being if he did not volunteer---that he would like his life, even perhaps his death, to count for something. The children and I could not argue with his reasoning, and we were totally united in his decision to volunteer.

I do believe that at no time in the history of human experimentation were the happenings and facts more openly and honestly presented than by Dr. Chase Peterson---both the good times and the hard times. Never, do I believe, did a group of people respond more conscientiously, with individual effort, to make an experiment successful, and never, in my experience, have I witnessed the peoples of the world respond with such hope, with such enthusiasm, and with such caring. Though my dear husband lived but 112 days, each of those 112 days were productive in furnishing something of human and spiritual value and myriads of medical knowledge. Though he did not receive the enduring personal benefit he hoped for, he did receive satisfaction in the knowledge he had been the vehicle through which a medical breakthrough of great magnitude was accomplished---opening the door through which four other courageous men have now followed and made tremendous contributions. To these men---Mr. William Schroeder, Mr. Murray Haydon, Mr. Jack Burcham and Mr. Lief Steinberg, and their fine families, I express my deep respect and my admiration.

Having met and associated with each of these fine men and their families, with the exception of Mr. Steinberg of Sweden, and through our conversations, I believe---although this has been a most difficult time through which they have gone, and are going, they realize the possibilities the artificial heart provides in the future, and are constantly striving to do their very best for the sake of those who will one day reap the benefits of their sacrifice.

During the three years since the first implantation, this technology has been thoroughly criticized, scrutinized, challenged, accepted as "hopeful" by some and threatened with abandonment by others. I am told that in an imperfect world, inhabited by imperfect people, this is a "healthy atmosphere" in which to work----Nevertheless, I have been gravely disappointed in the lack of patience and the lack of vision manifested in a technology which means so much to so many, in the rigidity of the rules and regulations imposed upon it and its Investigator and in the denial of permission to other very well-qualified Surgeons and their institutions to participate in this experimentation. I realize full well that definite guidelines are essential and that the number of investigators must be very restricted, but in a study such as this, surely it would be wise to employ the techniques, innovations and medical and scientific in-put of more than one Investigator. Of course, I am referring to the implantation of the Permanent Total Artificial Heart, as I realize many have been afforded permission to implant the artificial heart as a "bridge to transplant."

Three of the major criticisms of this experiment have been "Informed Consent", "Quality of Life" and the "Moral-ethical" issue.

As to "Informed Consent"---Dr. Clark and I felt we had been made as fully cognizant of the risks involved as was humanly possible within the realm of knowledge concerning it in its first application. Noone offered us any promises whatsoever; the burden of the decision was ours alone and in no way were we coerced into volunteering.

"Quality of Life" is a very flexible term and can be present in varying degrees to people under different circumstances and periods in their lives. My husband certainly did NOT have a reasonable quality of life before his implant---nor did he have a Quality of life he could enjoy after the implant, but he was willing to continue in the experiment as long as God gave him life to do so because he BELIEVED THERE WAS A PURPOSE IN IT---that purpose was to furnish medical knowledge to perfect a technology that he believed had possibilities of insuring a "Good Quality of Life" for many who might come after him.

As to the "Moral-Ethical Issue"---This, I believe, is a very personal judgment and can, in no way, be decided justly and fairly by a Committee or Group. This judgment emerges from our individual views as to right to life, desire to preserve life and from our deep-seated personal beliefs. It is our belief, Dr. Clarks, my families and mine, that God's greatest gift to us is the gift of life and the innate intelligence he endowed us with---hopefully to progress in all things. We believe that our desire to protect and prolong life is a manisfestation of our appreciation for that gift, and is a form of progression. Therefore, we had no problem with the moral-ethical aspect of the artificial heart and believe this question cannot be ruled upon justly by the community as a whole until AFTER investigators have been given ample time to resolve the problems that exist at this early stage of the experiment.

Having had the opportunity to play a supportive role to my dear husband and the Utah Heart Team as they accomplished this medical breakthrough, and having had the privilege of serving the American Heart Association during the past 2½ years---fully realizing that although we are making in-roads in the treatment and prevention of heart disease, it is still responsible for more deaths than all other causes combined, I am deeply grateful to have been involved in the fight against heart disease.

I am excited with the success experienced through the technology of donor heart transplants----but I am deeply concerned about those not considered as candidates for this therapeutic treatment, about the shortage of donor hearts and about the thousands of people who die awaiting a donor heart. Therefore, I believe the further study of the Permanent Total Artificial Heart, and the Artificial Heart as a "bridge to transplant" is not only fully justified, but is essential to medical progress and our efforts to stem the tide of heart disease.

I thank God for men of vision and the pioneering spirit who posess the courage to face possible failure, but who exhibit the tenacity and perseverance to unrelentlessly seek ultimate success in this endeavor---Such men are those who have contributed thus far, and who are still contributing to the Artificial Heart experimentation.

* * * * *

Mrs Barney Clark

APPENDIX 6

DEPARTMENT OF HEALTH & HUMAN SERVICES
Office of the Secretary
Washington, D.C. 20201

5 1986

The Honorable Harold L. Volkmer
Chairman
Science and Technology Subcommittee
on Investigations and Oversight
House of Representatives
Washington, D.C. 20515

Dear Chairman Volkmer:

Enclosed is the edited transcript of Dr. Claude Lenfant, Director, National Heart, Lung and Blood Institute who testified at the February 5 hearing on artificial heart implants.

If we can be of further assistance, please let me know.

Sincerely yours,

Patricia Knight

Patricia Knight
Acting Deputy Assistant Secretary
for Legislation (Health)

Enclosure

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Dr. Claude Lenfant, Director
National Heart, Lung and Blood Institute
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Lenfant:

Enclosed is a copy of the transcript from the February 5, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight about artificial hearts. Attached to the transcript are instructions for submitting requests for changes or clarifications. Please review these instructions and the enclosed transcript of your remarks carefully. Your copy of the transcript, together with any written requests for changes, should be returned by April 24, 1986 to:

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mail to

Dr. Irene Glowinski
Subcommittee on Investigations and Oversight
822 House Annex I
Washington, DC 20515-6307

Your testimony at the hearing was extremely valuable to the Members, and I want to extend our thanks for your participation and service to the Subcommittee.

Sincerely,

Harold L Volkmer

Harold L. Volkmer
Chairman
Subcommittee on Investigations
and Oversight

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Just a moment, does somebody have a time constraint?

Well, let's see, Dr. McIntosh, Dr. Lenfant, you have any time constraints. I know you would like to get out of here as soon as possible. Everybody would like to do that.

But other than that do you have to be somewhere besides back at the office?

Would you be agreeable with us proceeding with Mr. Morris at this time?

VOICE. Oh, certainly.

Mr. VOLKMER. All right then, fine, we will proceed in that method then.

STATEMENTS OF CLAUDE LENFANT, M.D., DIRECTOR, NATIONAL HEART, LUNG AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH; CHARLES L. McINTOSH, M.D., Ph.D, CHAIRMAN, CIRCULATORY SYSTEM DEVICES ADVISORY PANEL, U.S. FOOD AND DRUG ADMINISTRATION; AND JOHN A. NORRIS, J.D., M.B.A., DEPUTY COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, U.S. PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY: DR. KSHITIJ MOHAN, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

STATEMENT OF DR. CLAUDE LENFANT

Dr. LENFANT. Mr. Chairman, I propose to be fairly short since my full written statement will be introduced in the record.

What I would like to do is briefly describe ~~the~~ my statement and highlight ~~some of the~~ the points.

Our statement ~~describes~~ discusses six ~~groups~~ areas.

First, we describe the artificial heart program since its beginning.

~~And~~ Next we describe how ~~the~~ resources are allocated to this program, which is only one of the many programs our Institute sponsors.

~~We will discuss how we assess and give you the programs, and you might be interested to know, Mr. Chairman, that in the 22 years of existence of the program we have had nine full-fledged scientific figures, the last one being summarized in this report which has given to the committee.~~

My statement also ~~describes~~ discusses ethical considerations, alternatives to heart replacement; and some aspects of risk and quality of life.

Of all these issues I would like to highlight a few points, ~~and~~ most importantly the evolution of the program since it was created some 22 years ago. ~~And~~ Indeed, the program started in 1963, under Congress' impetus, which ~~in fact~~ in 1964 ~~decided to~~ ~~introduce~~ established a line in the budget of the Institute, and appropriated the specified amount of $600,000.

In the 60's and early 70's, some ~~great~~ important milestones resulted from the program, not least was the development ~~[illegible]~~ of blood oxygenators, and intra- vascular balloons, which are ~~[illegible]~~ devices that ~~[illegible]~~ are now part of ~~[illegible]~~ everyday clinical care.

As well ~~[illegible]~~ short-term circulatory assist devices were developed and since have been used quite extensively, mostly in the support of patients in the post-surgical phase of their treatment.

In the early 1980's we focused our program on the development of components for an electrically powered ventricular assist system, and, of course, on the Jarvik-7 artificial heart, which was discussed at length this morning. ~~reached maturation, and~~ Many of these devices have since moved from ~~the develope~~ model testing into clinical applications.

As you know, five ~~[illegible]~~ total heart ~~[illegible]~~ replacements have been done with the Jarvik model. ~~this device,~~ ~~[illegible]~~. Temporary bridge-to-transplant applications have been made using the Jarvik and other devices, as well.

Currently, we are testing some new devices, one is here, for instance. These new devices are ~~[illegible]~~ fully implantable devices; they can be used as ~~[illegible]~~ single ventricule. or eventually a fully implantable artificial heart.

Having described briefly the history of the program I would like to mention how we are allocating resources to it. As I said, the first allocation of ~~[illegible]~~ resources were made specifically ~~[illegible]~~ by Congress in 1964 to create the artificial heart program.

~~[illegible]~~ Since then the Institute ~~[illegible]~~ has regularly allocated ~~[illegible]~~ funding each year from ~~[illegible]~~ its regular appropriation for the program. ~~[illegible]~~. In 1967 this amount reached $8 million; in 1974, it reached about $12 million a year; and the same amount has been allocated to this program since, with an exception in 1976 when we were allocated as much as $15 million.

It may be of interest to you, Mr. Chairman, that three-quarters of this amount is given to investigators ~~[illegible]~~ through the contract mechanism; in other words, it is a ~~[illegible]~~ targeted program of the Institute. The last ~~[illegible]~~ quarter ~~[illegible]~~ is in the form of grants to investigators who submit applications for us. These applications are reviewed ~~[illegible]~~ through our peer review system.

Let me me now briefly mention, the process that we utilize to ~~[illegible]~~ determine what amounts of money will be allocated to this program.

When ~~[illegible]~~ the program was first started most of the advice given to the Institute came from ~~[illegible]~~ ad hoc consultants which were called in whenever needed. ~~[illegible] provide advice and, again, ad hoc, somewhat spotty~~ ~~[illegible]~~

Since 1974, the Institute has greatly relied on a more formalized process which includes the Cardiology Advisory

Committee. This ~~the~~ body of experts includes ~~in~~ cardiology and other disciplines. ~~[illegible]~~ It advises ~~[illegible]~~ the Institute on the ~~[illegible]~~ overall ~~cardiology~~ heart research ~~[illegible]~~ program of ~~[illegible]~~, of which the artificial heart program is only one component.

The advice of this ~~[illegible]~~ body, the Advisory Cardiology Committee, goes to the National Heart, Lung, and Blood Advisory Council, which is another body made up of the scientific experts ~~[illegible]~~ as well as leaders in non scientific fields. ~~[illegible]~~.

Using ~~with all this~~ std. advice ~~[illegible]~~ first from the Cardiology Advisory Committee, and then from the National Advisory Council, the Director of the Institute makes a final decision as to the allocation of resources to the various programs of the Institute.

I think it is important ~~[illegible]~~ to emphasize that the Institute has many competing priorities. This morning when we started these hearings, some health statistics were given to you, that ~~[illegible]~~ indeed, about half of the deaths in this country each year are due to cardiovascular diseases. If we take all the diseases which are within the purview of our Institute, approximately 53 ~~[illegible]~~ to 56 ~~[illegible]~~ percent of all the deaths in the ~~[illegible]~~ country are due to diseases which are within our the scope of our mission ~~purview~~.

Finally, I should speak about the ~~say that, sir, with regard to this, there is a~~ number of very significant spinoffs that have come from the artificial heart programs. I should mention [redacted] cardiovascular implants, such as artificial valves, the development of polyurethanes, an inert substance which is used in many prostheses and many other devices. The collagen-derived artificial skin is also a spinoff of the program. Also,

~~And finally,~~ materials which are used for the fabrication of contact lenses [redacted] and other devices, are a spinoff of our program.

To conclude my remarks, Mr. Chairman, I would like to emphasize that the Institute's mission is to foster and support a broad range of activities designed to reduce deaths and disability. We estimate that as many as 20,000 to 30,000 Americans suffer each year from heart failure. [redacted]

Our main goal is to prevent this condition from developing. But meanwhile, we feel that total heart replacement with a mechanical device has the [redacted] potential to become a std. viable treatment [redacted] alternative.

And, therefore, we continue [redacted] to support [redacted] the experiment which Dr. DeVries so ably [redacted] described. [redacted] Hopefully it will demonstrate whether [redacted] artificial heart surgery [redacted] has some value or not.

Thank you very much.

Mr. VOLKMER. Thank you very much, Dr. Lenfant.

[The statement of Dr. Claude Lenfant follows:]

********** INSERT 3 - 1 *********

devices that have been approved for that purpose--

Dr. MOHAN. As [illegible] bridge?

Mr. VOLKMER. As a bridge.

Dr. MOHAN. Yes.

Mr. VOLKMER. But not as experimental any longer?

Dr. MOHAN. Approved as an investigational device, not--

Mr. VOLKMER. That's what I mean.

Dr. MOHAN. --not approved for marketing.

Mr. VOLKMER. Not approved for market. We don't have any approved for market? That's what I meant.

Dr. MOHAN. No, no.

Mr. VOLKMER. All right.

Does anyone, Dr. McIntosh or Dr. Lenfant, want to comment on that last statement before, as to the LVADs, all of them being experimental, none could be better than the other, at this time?

Dr. LENFANT. Two of the models which are here have been approved for clinical testing; these two.

And you also asked if some were in a development phase. These two are in a development phase.

Mr. VOLKMER. All right.

At this time I am going to recess. Mr. Morris, if we have any additional questions, I think we should direct them solely to you. We will submit them in writing, all right? If not, we will continue when we return.

show that change--

Mr. VOLKMER. And it would be fair to say that each proposed change you would have to make the decision based on that proposed change, and you can't really make a general statement, complete general statement.

Dr. MOHAN. That's right.

Mr. VOLKMER. All right.

Dr. Lenfant, as I understand it, clinical trials of the electrically powered left ventricular assist device--and I believe you have that, one of those devices there, do you not--is scheduled to begin in 1987. Is that correct?

Dr. LENFANT. That's correct, Mr. Chairman.

Mr. VOLKMER. What information are we expecting to learn from these trials?

Dr. LENFANT. Let me back track a bit and say that just now we are ~~being~~ bench testing ~~with~~ the device. Once this testing ~~[illegible]~~ is completed and we are satisfied we are dealing with a reliable device ~~on a bench~~ then we move to the next phase, which is ~~using this device in~~ human clinical applications to ~~[illegible]~~ assess whether the match of the device and the patient is ~~[illegible]~~ workable, reliable and effective.

Mr. VOLKMER. Is NIH funding any of the clinical evaluation of the pneumatic systems?

Dr. LENFANT. ~~No. We have done the supported the work o~~n

Are you referring to the Jarvik heart?

Mr. VOLKMER. No. I am talking about the electrically powered--oh, it is the Jarvik, all right. You're not on the Jarvik heart?

Dr. LENFANT. The answer to that is no, not for the Jarvik.

Mr. VOLKMER. All right. And why? Can you tell us why not?

Dr. LENFANT. Well, because basically the device moved into clinical application~~s~~ by decision of ~~the private sector~~ Dr. DeVries himself. And there was really no consultation between us and Dr. DeVries at that time. ~~And~~ Our feeling was that he felt he was ready to do it. Therefore, if the private sector is willing to engage in this kind of activity, we feel that we have no reason to provide support.

Mr. VOLKMER. In other words, if the private sector starts into it, what I am seeing then, you tell me if the private sector proceeds with something on their own and it progresses to a certain stage, then NIH is not going to come in and help out?

Dr. LENFANT. That's correct, especially for clinical applications.

Mr. VOLKMER. All right.

Well, before I go to full panel questions, I will yield to something, I believe, about the informed consent from the patien''s standpoint as well.

Mr. PACKARD. Dr. Lenfant.

Dr. LENFANT. Yes, I just would like to add to the second part of your question, that is, whether there are ~~some~~ the same ~~[illegible]~~ complications with heart transplants. The complications are not the same ~~[illegible]~~, but there are some complications with heart transplant. Basically you have to walk a very thin line between rejection, on the one hand, and infection, on the other hand. One of these complications, rejection, is controlled by drugs such as cyclosporin, which I am sure you heard of. And the regulation ~~administration~~ of this ~~that~~ drug is ~~[illegible]~~ under the aegis of the Food and Drug Administration ~~for that particular purpose~~. I don't know if it has passed the experimental phase. I guess it has.

But cyclosporin is a drug which brings about some complications in itself, that is, kidney alterations and in some cases elevation of blood pressure.

Mr. PACKARD. Thank you.

Has the--rather, under what circumstances would FDA deny the use of the artificial heart, knowing or assuming there's no other alternatives and that the patient would die without the use of such device? Under what circumstances would normally you put a hold or a stop on the use of it, particularly in light of clinical experience?

one a year and a half, two years. And we have very few strokes. And they are ambulatory and everything else is going great. And sometime in the future they are approved for marketing. Now, the question I have is, what are the costs going to be, and who is going to pay for it? Because on permanent transplants right now, we only have, you know, the ones being done at Humana; and we know who's paying for those. Those costs are running astronomical. I am sure some of those costs will be able to come down as we do it. But who's going to pay for it?

Dr. LENFANT. Well, I don't know who is going to pay for it, but I can tell you how much it is going to cost. In our study this question ~~that aspect of the artificial heart~~ was considered quite carefully. The estimate, and you heard some figures today, is that there may be twenty to thirty thousand people a year who might be eligible to receive a chronic artificial heart. Although the cost, as you heard it from Dr. DeVries, is high today, there is an expectation that eventually it would go down to probably $150,000 a patient, for about a two-year survival period.

Now, if we multiply this by the number of patients, we are reaching an amount per year of $2.5 to $3 billion, which is, of course, a sizable amount of money. Who is going to provide this money, it is not mine to say. I might only repeat what was indicated in the report of our studies, that there are other similar long-term therapies which are in the same order of cost.

Mr. VOLKMER. Renal dialysis, which is--

Dr. LENFANT. For--

Mr. VOLKMER. --that costs, and the Federal Government is picking up a large chunk of that.

Dr. LENFANT. Yes. I surmise. I don't know for sure, but I surmise.

Mr. VOLKMER. So, that isn't part of the study, where the money is going to come from to pay for it.

Dr. LENFANT. I--

Mr. VOLKMER. I mean, there's not--

Dr. LENFANT. All I can tell you--

Mr. VOLKMER. There's not very many individuals, there are some in this country, but not very many individuals that are going to be able to come in and plunk down $100,000 or $150,000 for a permanent artificial heart transplant. We have to recognize that.

The second question is the question about, what about the insurance carriers, whether they would do it. And if they do it, I'll guarantee you everybody's premiums are going to go up some.

Dr. LENFANT. Well, I am not in a position to answer this question either personally or on behalf of the--

Mr. VOLKMER. Does anybody else wish to comment on it at all?

Dr. MCINTOSH. I think you're absolutely right. In the beginning, the transplantation procedures, the heart, were not covered by insurance, and they are now. If it realistically comes down to a price equivalent to a transplant, then I think the question becomes perhaps a little less important. If we can put an artificial heart in somebody for the same price that we can transplant somebody, that may be a key issue. And I don't know the answer to that.

Mr. VOLKMER. Dr. Lenfant, in your study we don't get that far down, do we?

Dr. LENFANT. No, we don't.

Mr. VOLKMER. I have one that I asked the staff to make sure I didn't forget, and then I did forget.

Dr. Lenfant, Gramm-Rudman, 4.3 reduction, March 1, approximately 20, 25 percent reduction, October 1 for the following year. What does that do to all these programs and all these devices that you have here and others?

Dr. LENFANT. Well, I think it's premature for me to answer this question, Mr. Chairman. As you saw from the documentation that we submitted to the committee, the Institute has been providing approximately $12 million a year to this program for a number of years. We feel that it is an adequate and appropriate amount of money. If nothing was to change today, we would probably not change that allocation either up or down.

With the implementation of Gramm-Rudman legislation and the President's budget, I don't know what we are going to do relative to this particular program. It is premature for me to answer that question.

But I would like to submit to the Committee that our Institute has many, many priorities. This one, the priority of this program, is not the lowest; but it's not the highest, as well. So, therefore, with our National Advisory Council and all the experts in the field who are advising us, we will try to do the best we can.

Mr. VOLKMER. I am assuming everybody in the government, I hope, will do the best they can. But still it would have an impact on some of the programs if you do receive, let's say, a reduction next year in funding for all your programs of $3 million.

Dr. LENFANT. I think it is quite reasonable to assume that this one will have to participate in this reduction.

Mr. VOLKMER. Mr. Mohan, FDA, if you receive a reduction next year of 20 to 25 percent in funding to administer these programs and have a review, et cetera, of these programs, how does that impact on the programs?

Dr. MOHAN. It's a little difficult to anticipate exactly what might happen. Again, those decisions are being made in